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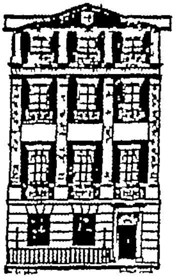

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| Pages | Date of Issue | No | Pages | Date of Issue | No | Pages | Date of Issue |
|---|---|---|---|---|---|---|---|
| 1–58 | Jan 1 | 6853 | 467–520 | March 5 | 6862 | 929–980 | May 7 |
| 59–110 | ,, 8 | 6854 | 521–574 | ,, 12 | 6863 | 981–1032 | ,, 14 |
| 111–160 | ,, 15 | 6855 | 575–628 | ,, 19 | 6864 | 1033–1082 | ,, 21 |
| 161–212 | ,, 22 | 6856 | 629–682 | ,, 26 | 6865 | 1083–1134 | ,, 28 |
| 213–262 | ,, 29 | 6857 | 683–730 | April 2 | 6866 | 1135–1184 | June 4 |
| 263–314 | Feb 5 | 6858 | 731–776 | ,, 9 | 6867 | 1185–1232 | ,, 11 |
| 315–362 | ,, 12 | 6859 | 777–826 | ,, 16 | 6868 | 1233–1282 | ,, 18 |
| 363–416 | ,, 19 | 6860 | 827–876 | ,, 23 | 6869 | 1283–1336 | ,, 25 |
| 417–466 | ,, 26 | 6861 | 877–928 | ,, 30 | 6870 | | |

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II—WATER LOAD RESPONSE IN HYPOTHYROIDISM (BEFORE AND AFTER TREATMENT)

| Time and volume of urine | Initial response | Corticotrophin (units × days) | Thyroid (dosage × days) | |
|---|---|---|---|---|
| | | 100 × 7 | Thyroxine 0·1 mg × 21 | |
| 2nd hr (ml. per min.)<br>3-hr total (%) | 1<br>28 | 1·5<br>16 | 2·0<br>38 | |
| | | 60 × 7 | | |
| 2nd hr (ml per min.)<br>3-hr total (%) | 10·5<br>90 | 15·8<br>100 | | |
| | | | Thyroid gr 3 × 7 | |
| 2nd hr (ml per min )<br>3 hr total (%) | 4·5<br>48 | | 8·[illegible]<br>90 | |
| | | | Thyroid<br>gr 3 × 27 | gr 3 × 31 |
| 2nd hr (ml. per min.)<br>3 hr total (%) | | | 3·5<br>60 | 7·5<br>95 |

be completed until after twenty-seven days thyroid py but even then it gave less than the normal response.

## Endocrine Assays in Hypothyroidism

these 4 patients with hypothyroidism the adreno cal function was normal in the 1st, a low normal in the deficient in the 3rd (who had been without thyroid py for six weeks only), and grossly deficient in the In each patient the output of 17 ketogenic steroids increased by thyroid therapy and the two deficient nts reached normal levels

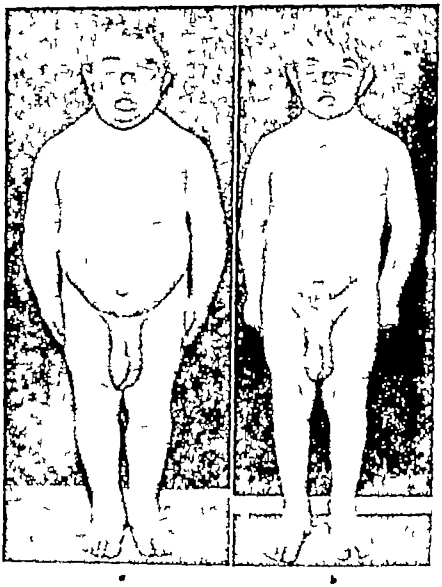
he response of the adrenal cortex to *corticotrophin* tested in 3 patients In the 1st patient the normal ex was fully responsive in the 2nd patient after n days treatment with corticotrophin 60 units y the depressed cortex was moderately responsive ketogenic steroids from 5 mg to 15 mg per 24 hr ), e 3rd patient, after thirty five days thyroid therapy seventeen days treatment with corticotrophin nits daily the partially recovered cortex was capable a moderate response (17 ketogenic steroids from to 13 mg per 24 hr ) Adrenocortical function is efore sometimes but not invariably depressed in cœdema. Statland and Lerman (1950) and Hill l. (1950) came to a similar conclusion In my cases adrenocortical depression was corrected by thyroid apy Beierwaltes and Bishop (1954) have found t the excretion of 17 ketosteroids by myxœdematous nen is subnormal and will usually increase to normal ls even over periods as short as one and a half nths if thyroxine dosage is increased sufficiently

his adrenocortical depression is sometimes regarded the direct effect of hypothyroidism on the adrenal tex— myxœdema of adrenocortical tissue, though tland and Lerman (1950) observe that this depression y be the result of disturbed pituitary function In f the 3 patients described above who were stimulated h corticotrophin the depressed adrenal cortex was able of response while the patients were still hypo roid The response was however far from normal l the central problem remains unsettled for this tial response may indicate that the adrenal cortex sluggish either because it suffers from thyroxine lack because it has been deprived for so long of its nor l stimulus to activity—corticotrophin Indeed both chanisms may be concerned It is certainly possible t the output of corticotrophin is sometimes depressed hypothyroidism

## Water-load Response

In case 3 the water load response was grossly defective d although she might not have fully recovered from her cardiac failure at that time the water load response was still not normal after twenty-one days thyroxine therapy when cardiac failure had long disappeared Throughout this time adrenocortical function was normal or better than normal (stimulated by corticotrophin) In case 4 despite severe and prolonged myxœdema and mild adrenocortical depression, the water load response was fully normal In case 5 in whom myxœdema had followed thyroidectomy and who had been without thyroid therapy for no more than six weeks the water load response was subnormal Both the response and adrenocortical function were improved by a week's thyroid treatment In the cretin (case 6) the water load response was still defective after twenty seven days thyroid therapy but was fully restored after thirty four days treatment

The water load response in myxœdema has been reported to be normal Levy et al (1946) investigating the response to the Kepler test in conditions other than Addison's disease reported a normal response in 3 patients with myxœdema It should be emphasised that the criteria for the Kepler test are not identical with those for the water load response as defined above Gaunt et al (1944) report a normal diuretic response in rats made hypothyroid with thiouracil. Garrod and Burston (1952) refer to unpublished observations in which patients with myxœdema gave a normal diuretic response † However the subject has recently been reopened by Crispell et al (1954) who report a delayed diuretic response in 8 patients with myxœdema This delay was corrected with thyroid sometimes after long continued treatment but in 4 of 5 patients was not corrected with cortisone Those workers conclude that the delay in



Cretin aged 25 showing excessive genital development: a on Feb. 16, 1954, before treatment; b on April 2, 1954, after treatment.

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† Since this paper was submitted Garrod and Gilliland have reported that 16 of 18 cases of myxœdema in response to the standard water load exceeded 3 ml per minute and 60 excretion while the other 2 patients showed a poor diuresis (*Proc R Soc Med* 1954 47 880)

diuresis in myxœdema is not caused by hypo adrenalism, and observe that their results allow no conclusion about whether this delayed diuresis is associated with the depression of glomerular filtration-rate which is known to occur in myxœdema (Corcoran and Page 1947, Davies et al 1952) or with increased tubular reabsorption My results confirm that there may be delayed diuresis in myxœdema which is corrected by thyroid therapy but is not restored by improved adrenocortical function

This finding of a defective water load response in hypothyroidism, which conflicts with the previous reports of other workers (although retention of water is a classical feature of myxœdema), could be attributed to the presence of unrecognised cardiac failure It is appreciated that the differential diagnosis between myxœdema with retention of water and myxœdema with congestive cardiac failure may not be easy, indeed much has been written to illustrate this difficulty It is not thought that any of the patients reported here were in cardiac failure when the defective water load response was demonstrated

## The Pituitary in Hypothyroidism

The possibility that hypothyroidism may lead to a decrease in output of corticotrophin from the anterior lobe of the pituitary gland suggests an inquiry into pituitary function in hypothyroidism It is well established that, in the absence of thyroxine, the output of thyroid stimulating hormone is greatly increased This is matched by cellular hyperplasia in the anterior lobe of the pituitary gland Although enlargement of the pituitary gland has often been reported in myxœdema, adequate studies, using modern techniques, of the results of thyroidectomy and of thyroid aplasia on the pituitary gland are rare, therefore the observations of Crane et al (1954) on "thyroid ablated" monkeys are valuable They found that in these monkeys the anterior lobe of the pituitary gland was increased to twice its normal size, with hyperplasia of the beta cells That this excessive growth of tiss [illegible] myxœdema can occur in other situations w is also s [illegible] by my cretin (case 6) (see figure) in the presence of the [illegible]al skeletal retardation (height 3 ft 10 in and bone age 11–12 years) the penis, testes, and scrotum had grown beyond the average adult size The prostate gland was not certainly palpable, and there had been no seminal emissions Moreover, the institution of thyroid therapy stimulated not only androgenic output, shown by the growth of pubic hair (previously absent) and by the increased output of 17 ketosteroids (from 3 to 12 mg per 24 hr ), but also the output of pituitary gonadotropins from 0 to 6, 16, and 18 mouse units per 24 hr Although the output of follicle stimulating hormone was minimal at the time of admission to hospital, there was also ample clinical evidence of the production of anterior pituitary sex hormones The adrenal androgens were unawakened, and possibly the stimulation of luteinising hormone had been lacking It is evident that in this man hypothyroidism, with the increased production of thyroid stimulating hormone, had caused some dissociation in the formation of the pituitary sex hormones It is also evident that thyroxine is not essential for the growth of cells when there is an adequate supply of the tropic hormone

Paschkis et al (1954) report that myxœdematous women of childbearing age often have menorrhagia and metrorrhagia and sometimes polycystic ovaries and endometrial hyperplasia They suggest that these changes may result from the increased output of gonadotropins (follicle stimulating hormone) Hypothyroidism, therefore, can disturb the production of anterior pituitary [illegible] and although its effects are still [illegible] excess or deficiency of individual [illegible] ult

## Endocrine Relations and Hypopituitarism

Since the endocrine relations of myxœdema are as complicated as I have suggested, it is not surprising that the endocrine relations in hypopituitarism are difficult to elucidate I have observed (Hubble 1952) that in anterior-pituitary deficiency, whatever the cause, sexual failure always precedes thyroid and adrenocortical failure which may be long delayed This has been accepted by other workers, and Peters et al (1954) suggest that thyroid failure follows sexual failure, and that adrenocortical failure is always the last to appear Though this observation may sometimes be correct, amenorrhœa in females, with loss of sexual hair, and loss of libido in both sexes indicate more or less definitely the onset of sexual failure, but the assessment of thyroid and of adrenocortical function has only recently become accurate

Many workers have commented on the fact that in hypopituitarism the blood cholesterol level provides an inadequate index of hypothyroidism, and that the basal metabolic rate (B M R ) may be reduced by other factors than a lack of thyroxine (Querido et al 1954, Peters et al 1954) Radio iodine studies and the estimation of protein bound iodine are providing much mor
accurate information about the function of the thyroid

Similarly it is important that in estimating adren
cortical function in hypopituitarism the tests used shou
be precise, sensitive, and specific Peters et al (195
reporting on the sequence of endocrine failure in
patients with hypopituitarism, are content with blo
sugar and serum electrolyte estimations as their in
of adrenocortical function The height of the bl
sugar level is not the result of a specific adrenocor
mechanism, and the estimation of serum electrolyte
reveal only a severe degree of adrenocortical defic
It is therefore not surprising that these workers c
report any case in which adrenocortical deficiency appeared before hypothyroidism declared itself

**Case 7** —A male patient, aged 61, with hypopituitarism associated with a large tumour (probably a craniopharyngioma) The B M R was –5%, the blood cholesterol level was 165 mg per 100 ml , the peak uptake of $I^{131}$ was 29% of the administered dose, and there was no clinical evidence of hypothyroidism Yet the water load response was not only grossly defective (2 8 ml per min in the second hour and 35% total excretion in three hours) but also was easily corrected with cortisone The output of 17 ketosteroids was 2 mg per 24 hr and of 17 ketogenic steroids 4 mg per 24 hr

Here, then, is one patient in whom the thyroid function is complete, by all available tests, while adrenocortical function is deficient Two patients of mine with post partum necrosis of the pituitary have also shown normal thyroid function with defective adrenocortical function

That the endocrine relations of hypopituitarism may still be obscure despite the use of these modern methods is illustrated by the following 2 cases

**Case 8** —A married woman, aged 45 Her menses started at the age of 17 Her only child was born in May, 1928, when she was aged 20 She had a normal confinement, and the baby was breast fed She has had no menses since Axillary and pubic hair had never been profuse but disappeared entirely in the next year or two Subsequently she became tired and sensitive to cold Myxœdema was diagnosed when she was aged 34, and she has taken thyroid gr 3 daily since Libido diminished at the age of 35 and quickly disappeared She presented the total picture of hypopituitarism on admission to the ward on April 27, 1954 Thyroid therapy was stopped two weeks before admission

*Investigations* —The output of urinary gonadotropin and
œstrogen, assayed on four occasions was nil , that of urinar
17 ketosteroids was 1 5 mg per 24 hr , and of urinary
17 ketogenic steroids 3 5 mg per 24 hr The $I^{131}$ peak uptake
was 5% of 23 6 µC The water load response was >1 ml pe
min in the second hour, and 17% in three hours Bi
chemical investigations were normal except for hype
cholesterolæmia The water load response was not corrected
by corticotrophin 60 I U × 7 or by cortisone 50 mg × 13

After treatment with thyroid gr. 3 × 37 and with cortisone 50 mg. × 40 the flow in the first hour was 4·6 ml. per min. and in the second hour 1·2 ml. per min., and the total in three hours was only 33%. Diuresis occurred seven hours after the water load. The patient is in perfect health with cortisone and thyroid therapy.

Case 9.—A married woman aged 50 had undergone fourteen years previously subtotal thyroidectomy for thyrotoxicosis. Her menses ceased at the same time. After an operation for thrombosed piles, five years ago, she had a severe uterine hæmorrhage, and since then she has suffered from fatigue, loss of libido, and sensitivity to cold. Pubic and axillary hair has disappeared during the last five years.

*Investigations.*—Urinary œstrogens were absent from three of four assays. Urinary gonadotropins were 6, 16, 40, and 70 mouse units per 24 hr. (these last two assays were made after thyroid therapy). Urinary 17-ketosteroids were 1·5, 3, 2·5, and 4 mg. per 24 hr., and urinary 17-ketogenic steroids 5, 4, and 7 mg. per 24 hr. The $I^{131}$ peak uptake was 7·2% of 20·1 μC. Biochemical investigations were normal except for hypercholesterolæmia. The water-load response was 3 ml. per min. in the second hour and 32% in three hours. The adrenal cortex was responsive to stimulation by corticotrophin. Neither thyroid nor cortisone fully corrected the water-load response: at the end of a month's therapy the flow was 3·2 ml. per min. in the second hour and the total excretion 50% in three hours.

*Comments*

Case 8 probably had pituitary inadequacy which developed gradually into total pituitary failure after her first and only confinement. Case 9 had postoperative myxœdema and an early menopause with partial adrenocortical failure, including androgen deficiency, after the uterine hæmorrhage five years previously. Both showed a gross defect of the water-load response, which was not corrected by cortisone but is being slowly restored by thyroid therapy.

The delayed diuresis in myxœdema may not be corrected until some months after adequate thyroid therapy has been instituted. This has been so in 2 of my patients and in some of the cases reported by Crispell et al. (1954). Corcoran and Page (1947) found that in 2 patients with myxœdema the renal blood-flow had not returned to normal after two and three months' treatment.

The conclusion to be drawn from these cases is that if adequate cortisone therapy in hypopituitarism has not corrected the delayed diuresis, this defect is associated with predominant hypothyroidism, whether primary or secondary. Thyroid therapy may then take some months to correct the defect. Cortisone restores the water-load response in hypopituitarism within a day or two if it is due to adrenocortical deficiency, whereas thyroid therapy in hypothyroidism restores the renal blood-flow much more slowly.

## Conclusion

One principle emerges from this investigation—i.e., when we are discussing endocrine relations we must not forget the pituitary. The controlling tropic mechanisms are there, control balanced by their target hormones, and no change takes place in the peripheral gland without its accompanying change in pituitary function. This pituitary change may concern not only an excess or a deficiency of the appropriate tropic hormone, but this in turn may cause an altered output of other tropic hormones. Hypothyroidism has been shown to illustrate this possibility.

The sequence of endocrine failure in hypopituitarism allows us another glimpse into the complicated functions of the pituitary. While the maintenance of thyroid and adrenocortical function after sexual failure has occurred may depend partly on the fact that these two glands are allowed some degree of "provincial autonomy," the evidence from endocrine assays suggests strongly that the sex hormones fail first, whatever the nature of the assault in the pituitary. Are they then the end product of cellular function, and is biosynthesis, when the pituitary faces destruction, carried no further than the formation of corticotrophin and thyroid-stimulating hormone? The chemists will one day tell us.

Meanwhile, some will say speculation is useless, and I might agree with them did I not believe that the modern insistence on peripheral mechanisms is obstructing our understanding. We are content to explain the association of thyrotoxicosis and diabetes by a peripheral mechanism—the effect of too much thyroxine on metabolism, on the beta-cells of the pancreas, and on hepatic glycogen—but I have here described 2 cases of diabetes and thyrotoxicosis in which there is evidence of hyperpituitarism—too much corticotrophin, too much growth hormone, and too much thyroid-stimulating hormone.

We may dislike Langdon Brown's notion of the pituitary as "the leader of the endocrine orchestra"—certainly a mechanism which can continue to prod a member of the band who is quite incapable of response while allowing other active members to languish for want of their essential stimulant hardly deserves the title—yet this does not justify us in forgetting that the pituitary must always be the centre of endocrine relations.

## Summary

The best test of adrenocortical function in excess or deficiency is provided by the Norymberski method for assay of the urinary 17-ketogenic steroids; the failure of adrenocortical function is well shown by a defect in the water-load response which is easily corrected with cortisone.

2 patients are described in whom coincidental thyrotoxicosis and diabetes were accompanied by overactivity of the adrenal cortex. It is suggested that these are examples of hyperpituitarism.

The adrenocortical function was depressed in 2 patients with hypothyroidism and was restored by thyroid therapy. There is evidence that this depression of adrenocortical function may be partly mediated through the anterior lobe of the pituitary gland, whose function may be variously deranged in hypothyroidism.

An impaired response to a water load was present in 3 patients with hypothyroidism and was gradually restored by thyroid therapy.

If the defective water-load response in hypopituitarism is not fully corrected with cortisone, a degree of hypothyroidism may be present requiring thyroid therapy which will slowly correct the defective water-load response.

The numerous endocrine assays were made in the Jessop Hospital for Women, Sheffield, and I am very grateful to Dr. G. O. Paine, Mr. L. F. Mitchell, PH.D., and Mr. M. J. Lovel, B.SC., for making this work possible. Miss A. Matthews, B.SC., Sister L. M. Edwards, and Sister J. E. Smedley controlled the laboratory and ward work with exemplary care.

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# CORTISONE IN EXOPHTHALMOS

## REPORT ON A THERAPEUTIC TRIAL OF CORTISONE AND CORTICOTROPHIN (A C T H) IN EXOPHTHALMOS AND EXOPHTHALMIC OPHTHALMOPLEGIA BY A PANEL APPOINTED BY THE MEDICAL RESEARCH COUNCIL*

THE conflicting reports of the value of cortisone and corticotrophin (A C T H) in exophthalmic ophthalmoplegia suggested the desirability of a larger inquiry into the usefulness of such treatment of a condition hitherto difficult of control The original interest was in examples of exophthalmic ophthalmoplegia of progressive or “ malignant ” type, but during the course of the trial patients with lesser degrees of proptosis and without ophthalmoplegia were also included The terms proptosis and exophthalmos are used interchangeably in this report

### Scope of the Study

28 patients were treated, 10 men and 18 women, whose ages ranged from 22 to 79 years One case (no 11, table II) features twice in some of the tables, owing to an acute exophthalmic episode developing during the course of observation, and this must be borne in mind in relation to the statistical presentation in the tables.

*Thyroid Status*

Clinical impression of thyroid function, supplemented in many patients by estimations of basal metabolic rate and radio iodine studies, indicated coexisting thyrotoxicosis in 15 patients (53%) at the start of treatment In 12 patients (43%) thyroid status had either been normal throughout the illness or had become so unde

TABLE II—EFFECT OF CORTISONE AND CORTICOTROPHIN IN 28 PATIENTS WITH EXOPHTHALMOS AND/OR EXOPHTHALMIC OPHTHALMOPLEGIA

| Case no | Duration | Age | Sex | Type and severity of exophthalmos | Ocular muscle function | Thyroid status | Drug and dosage | Effect of treatment |
|---|---|---|---|---|---|---|---|---|
| 1 | 2 months | 63 | M | Without chemosis<br>Proptosis moderate | R.S R and R.I O paretic | Euthyroid | C 200 mg daily for 21 days | Ophthalmoplegia Unchanged<br>Exophthalmos Slight improvement.<br>Thyroid function Depressed ($I^{131}$) |
| 2 | 1 year | 31 | M | Without chemosis<br>Proptosis moderate | R.S O paretic | Thyrotoxic | C 200 mg daily for 21 days | Exophthalmos Temporary improv ment<br>Ophthalmoplegia Area of diplop decreased<br>Thyroid function Thyrotoxicosis con trolled ($I^{131}$) |
| 3 | 1 year | 46 | F | Without chemosis<br>Proptosis moderate | R.S O paretic | Thyrotoxic | C 200 mg daily for 14 days | Exophthalmos Slight improvement.<br>Ophthalmoplegia Unchanged<br>Thyroid function Some depression ($I^{131}$) |
| 4 | 7 months | 32 | F | Without chemosis<br>Proptosis moderate | Normal | Thyrotoxic | C 200 mg daily for 11 days | No effect on exophthalmos or thyroid function |
| 5 | 18 months | 44 | F | Without chemosis<br>Proptosis moderate | Normal | Thyrotoxic | C 50 mg daily for 31 days | Exophthalmos Increased<br>Thyroid function Temporary remission—subsequent relapse ($I^{131}$) |
| 6 | 1 year | 55 | M | With chemosis<br>Proptosis moderate | Normal | Thyrotoxic | C 100 mg daily for 21 days | No effect on exophthalmos or thyroid function |
| 7 | 6 years | 55 | M | With chemosis<br>Proptosis moderate | E R S R, and I O paretic both eyes | Thyrotoxic | A C T H 100 mg daily for 15 days | Exophthalmos Marked improvement<br>Ophthalmoplegia Improved<br>Thyroid function Thyrotoxicosis con trolled (B M R)<br>Local effect Chemosis lessened |
| 8 | 6 years | 49 | M | Without chemosis<br>Proptosis slight | R E R paretic | Euthyroid | C 100 mg daily for 17 days<br>Na intake 800 mg daily | No effect on exophthalmos ophthalmoplegia, or thyroid function |
| 9 | 7 years | 65 | F | With chemosis<br>Proptosis severe | R.S R and L.S R paretic | Euthyroid | C 100 mg daily for 24 days<br>Low-sodium diet | Exophthalmos Marked improvement<br>Ophthalmoplegia Temporary improvement<br>Thyroid function Depressed (B.M.R.)<br>Local effect Improvement in chemosis |
| 10 | 1 year | 79 | M | With chemosis<br>Proptosis moderate | R.S.R and L.S R paretic | Euthyroid | C 100 mg daily for 33 days<br>Low sodium diet | Exophthalmos Slight improvement.<br>Ophthalmoplegia Unchanged<br>Thyroid function Unchanged<br>Local effect Improvement in chemosis |
| 11a | 9 months | 50 | F | Without chemosis<br>Proptosis moderate | S R paralysed E R paretic both eyes | Thyrotoxic | C 100 mg daily for 37 days | No effect on exophthalmos or ophthalmoplegia Thyrotoxicosis controlled (B M R) |
| 11b | 1 day | ” | ” | With chemosis<br>Proptosis severe | Complete ophthalmoplegia | Euthyroid | A C T H 100 mg daily for 18 days<br>Low sodium diet | Exophthalmos Dramatic improvement<br>Ophthalmoplegia Marked improvement<br>Thyroid function Unchanged<br>Local effect Marked improvement |
| 12 | 10 months | 70 | F | With chemosis<br>Proptosis moderate | R.S R and R I O paretic | Thyrotoxic | A C T H 100 mg daily for 21 days | No effect on exophthalmos ophthalmoplegia or thyroid function<br>Improvement in chemosis |
| 13 | 1 year | 25 | F | Without chemosis<br>Proptosis slight | Normal | Euthyroid | C 100 mg daily for 31 days | No effect on exophthalmos or thyroid function |
| 14 | 4 months | 57 | M | With chemosis<br>Proptosis severe | I O and S R both eyes | Thyrotoxic | A C T H 100 mg daily for 21 days | Exophthalmos and ophthalmoplegia worse<br>Thyroid function Unchanged<br>Local effect Improvement in chemosis |

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* The members of the panel were

Sir RUSSELL BRAIN (chairman)
Dr K ATERMAN
Dr C L COLE
Prof D M DUNLOP
Dr T RUSSELL FRASER
Dr RAYMOND GREENE
Dr E E POCHIN
Dr E F SCOWEN
Dr W R TROTTER
Prof E J WAYNE
Prof S J HARTFALL (secretary)

TABLE I—SEVERITY OF EXOPHTHALMOS AND INCIDENCE OF OPHTHALMOPLEGIA AMONG 28 PATIENTS SUBDIVIDED INTO THOSE WITH AND THOSE WITHOUT CHEMOSIS

| Type of exophthalmos | Severity of exophthalmos | | | No. of patients with ophthalmoplegia | No. of patients without ophthalmoplegia |
|---|---|---|---|---|---|
| | Slight | Moderate | Severe | | |
| With chemosis | 0 | 10 | 5 | 12 | 3 |
| Without chemosis | 4 | 10 | 0 | 7 | * |
| Total | 4 | 20 | 5 — 29 | 19 | 10 — 29 |

* One case (no. 11) features twice owing to an acute exophthalmic episode controlled with corticotrophin, developing during the course of observation following an initial period of treatment with cortisone

the influence of antithyroid drugs or surgery. One patient (case 27) was subthyroid

*Exophthalmos, Ophthalmoplegia, and Chemosis*

For purposes of classification severity of exophthalmos has been graded as slight, moderate, or severe, a distinction made on clinical grounds as well as by measurements of proptosis (for the exophthalmometer cannot record exophthalmos as an absolute). Consideration was given to the use of the terms 'fatty' and 'œdematous' but our criteria have only enabled us to state whether the cases have chemosis and œdema or whether these features were absent. The cases are therefore divided into those with chemosis and those without this feature.

The distribution of the types of exophthalmos (i.e. their severity) and the existence of ophthalmoplegia, together with the presence or absence of chemosis among the patients studied, is shown in table I. It will be seen that weakness of the extrinsic ocular muscles complicated the exophthalmos in 18 of the 28 patients. The table shows that patients with chemosis have, on the average, a more severe degree of exophthalmos and more paralysis than patients without chemosis.

## Treatment

In general, cortisone was given in the usual dosage (table II). It is notable that no side-effects from hypercorticism have been seen in this series. Cortisone has been used in 23 patients and corticotrophin in 5 patients (excluding cases 16 and 18, which had small doses of

TABLE II—(*continued*)

| Case no. | Duration | Age | Sex | Type and severity of exophthalmos | Ocular muscle function | Thyroid status | Drug and dosage | Effect of treatment |
|---|---|---|---|---|---|---|---|---|
| 15 | 3½ years | 38 | F | Without chemosis<br>Proptosis moderate | Diplopia on upward movement | Euthyroid | C 200 mg. for 2 days,<br>C 100 mg. for 11 days,<br>C 150 mg. for 4 days | No effect on exophthalmos, ophthalmoplegia, or thyroid function |
| 16 | 5 years | 38 | F | Without chemosis<br>Proptosis moderate | Normal | Euthyroid | C 200 mg. for [illegible] days<br>C 100 mg. for 10 days<br>C 200 mg. for 4 days<br>A.C.T.H. 37.5 mg. for 2 days | No effect on exophthalmos or thyroid function |
| 17 | 10 months | 22 | F | Without chemosis<br>Proptosis moderate | Normal | Thyrotoxic | C 200 mg. for [illegible] days<br>C 100 mg. for 9 days<br>C 200 mg. for [illegible] days | Exophthalmos: Unchanged<br>Thyroid function: More hyperthyroid (B.M.R.) |
| 18 | 1½ years | 68 | M | Without chemosis<br>Proptosis slight | Normal | Euthyroid | C 100 mg. for 13 days<br>C 200 mg. for 5 days<br>A.C.T.H. 25 mg. for 2 days | Exophthalmos: Increased |
| 19 | *18 months* | 47 | M | *With chemosis*<br>Proptosis moderate | *L.E.R. paretic* | *Thyrotoxic* | *A.C.T.H. 50 mg. daily for 21 days* | *Exophthalmos: Unchanged*<br>Thyroid function: Thyrotoxicosis worse (B.M.R.)<br>Local effect: Chemosis improved |
| 20 | 17 years | 39 | M | With chemosis<br>Proptosis severe | L.E.R. and R.E.R. paretic | Euthyroid | C 200 mg. daily for 4 days<br>C 100 mg. daily for 10 days | No effect on exophthalmos, ophthalmoplegia, or thyroid function. Local improvement in chemosis |
| 21 | 7 months | 30 | F | With chemosis<br>Proptosis severe | Diplopia upwards and downwards | Thyrotoxic | C 100 mg. for 8 days<br>C eyedrops | No effect on exophthalmos, ophthalmoplegia, or thyroid function<br>*Local effect: Slight improvement* |
| 22 | 2 years | 38 | F | With chemosis<br>Proptosis moderate | Normal | Euthyroid | C 100 mg. for 6 days,<br>C eyedrops | No effect on exophthalmos, ophthalmoplegia, or thyroid function<br>Local effect: Slight improvement |
| 23 | 4 months | 27 | F | With chemosis<br>Proptosis moderate | Normal | Thyrotoxic | C 100 mg. daily for 21 days | No effect on exophthalmos.<br>Reduction in thyroid function (B.M.R.).<br>Local effect: Improvement in conjunctival œdema |
| 24 | 2½ years | 51 | F | Without chemosis<br>Proptosis moderate | Defective upward movement | Euthyroid | C 100 mg. daily for 21 days | *No effect on exophthalmos*<br>Thyroid function: Depression of hyperthyroidism (B.M.R.) |
| 25 | 1 month | [illegible] | F | Without chemosis.<br>Proptosis slight | Normal | Thyrotoxic | C 100 mg. daily for 21 days | Thyroid function: Thyrotoxicosis controlled (B.M.R.). No other change |
| 26 | 4 months | 41 | F | With chemosis<br>Proptosis moderate | Reduced | Thyrotoxic | C 100 mg. daily for 21 days | Exophthalmos: Slight improvement<br>Ophthalmoplegia: Unchanged<br>Thyroid function: Control of thyrotoxicosis (B.M.R.)<br>Local effect: Great improvement in chemosis |
| 27 | 18 months | 41 | F | With chemosis<br>Proptosis moderate | L.I.O. and L.S.O. paretic | Subthyroid | C 100 mg. daily for 21 days | No effect.<br>Local effect: Improvement slight |
| 28 | 3 months | 48 | F | With chemosis<br>Proptosis moderate | Limited up and out | Euthyroid | C 200 mg. 1st day, then 100 mg. daily for 23 days | Exophthalmos: No effect<br>Ophthalmoplegia: Unchanged<br>Thyroid function: Unaltered<br>Local effect: Definite improvement |

S.R. = superior rectus; E.R. = external rectus; I.O. = inferior oblique; S.O. = superior oblique; C = cortisone; A.C.T.H. = corticotrophin.
Where change in thyroid function was observed as a result of treatment the criteria by which this was measured—basal metabolic rate (B.M.R.) or radio-iodine studies (I )—are indicated.

corticotrophin for two days at the end of a course of cortisone treatment) The duration of treatment exceeded two weeks except in 3 patients (cases 4, 21, and 22), and averaged three weeks in the remainder

4 patients (cases 8–11) were given a diet providing a calculated daily sodium intake of 800 mg All other drugs were discontinued except in 1 patient (case 15), who received thyroid extract grains 2 daily throughout the period of cortisone administration

## Results

The details of treatment and its effect on proptosis and chemosis in individual patients are shown in table II The effect of treatment has been studied in relation to the following points

1 Effect on proptosis and ophthalmoplegia
2 Local effect on chemosis and œdema
3 Effect on thyroid function

### *Effect on Proptosis and Ophthalmoplegia*

The effect of treatment on proptosis has been classed under the following headings

1 Marked improvement—patients showing a reduction in exophthalmos of 5 mm or more in either eye

2 Slight improvement—patients showing a reduction in exophthalmos of 2–5 mm

3 No effect

The over-all results have been disappointing 3 patients (cases 7, 9, and 11b) showed a marked improvement, and 2 of these 3 patients who obtained a substantial degree of measurable benefit from treatment (cases 7 and 11b) received corticotrophin 5 patients (cases 1, 2, 3, 10, and 26) showed a more modest response, classed as slight improvement, which was temporary and not sustained The drug used in these was cortisone In no case has a permanent reduction in proptosis occurred and later relapse has always taken place In 3 patients (cases 5, 14, and 18) the exophthalmos slightly increased during treatment

Improvement in ocular muscle function occurred in parallel with regression of proptosis in 4 patients (cases 2, 7, 9, and 11) with consequent decrease in the area of diplopia It was notable that the muscles of elevation were usually the first and generally the most severely affected, and were also the first to show functional recovery

Improvement in chemosis was the most constant response and improvement has occurred in the 15 patients who showed this feature

Analysis of the results shows that improvement in proptosis was limited to those patients with ophthalmoplegia and was similar in the group with and the group without chemosis exophthalmos unaccompanied by ocular muscle weakness was uninfluenced by treatment (table III)

Table IV shows that there is a tendency for the proportion of patients showing improvement in exophthalmos to decline with increasing duration of the condition, but the numbers are too small for a firm conclusion to drawn The improvement in ophthalmoplegia was correlated with duration of the complaint

TABLE III—EFFECT OF TREATMENT ON EXOPHTHALMOS RELATED TO INCIDENCE OF OPHTHALMOPLEGIA

| Type of exophthalmos | Total no | Patients with ophthalmoplegia | | Patients without ophthalmoplegia | |
|---|---|---|---|---|---|
| | | No showing improvement in exophthalmos | No change or worse in exophthalmos | No showing improvement in exophthalmos | No change or worse in exophthalmos |
| With chemosis | 15 | 5 | 7 | 0 | 3 |
| Without chemosis | 14 | 3 | 4 | 0 | 7 |
| Total | 29* | 8 | 11 | 0 | 10 |

* Case 11 features twice

TABLE IV—EFFECTS UPON CHEMOSIS, EXOPHTHALMOS, OPHTHALMOPLEGIA IN RELATION TO THE DURATION EXOPHTHALMOS

| Duration | Chemosis | | Exophthalmos | | Ophthal plegia | |
|---|---|---|---|---|---|---|
| | No of cases | Improved | No of cases | Improved | No of cases | Im |
| Less than 6 months | 5 | 5 | 6 | 3 | 5 | 1 |
| 6 months–2 years | 6 | 6 | 13 | 3 | 8 | 1 |
| 2 years + | 4 | 4 | 10 | 2 | 6 | 2 |
| Total | 15 | 15 | 29* | 8 | 19* | 4 |

* Case 11 features twice

### *Effect of Treatment on Thyroid Function*

15 patients (53%) were hyperthyroid before tre ment, and after treatment the level of thyroid functi was depressed in 8 of these The improvement in thy toxicosis was attended in half of these patients by so improvement in exophthalmos, in those patients who thyroid hyperfunction remained unaltered by treatme no local benefit occurred The numbers are too few suggest any difference between the cortisone and cortico trophin groups It is possible upon occasion that modifica tion of coexisting thyrotoxicosis might be a factor bearing upon the success of treatment A study of the case records, however, shows no further evidence therapeutic indication, and it seems impossible to select in advance those patients with thyrotoxicosis who are likely to respond

Among 13 euthyroid patients some depression thyroid function was recorded in 3 cases under treatme

### *Effect of Sodium Restriction*

4 patients (cases 8–11) were given a diet providing daily sodium intake of 800 mg during the period administration of cortisone or corticotrophin Only patient (case 8) failed to derive objective benefit Sodi balance determinations did not show any clear evidence of a saline diuresis, though in general a negative sodium balance was established (Chandler and Hartfall 1952)

## Discussion

28 patients with exophthalmic ophthalmoplegia have been treated with cortisone or corticotrophin At the dosage used no beneficial effect was observed in patients, 5 showed slight temporary improvement and 3 responded well This difference in individual respo is reflected in the publications of other investigat (Lederer and Hambresin 1950) The reasons for the disparity are not immediately obvious, though a rec report (Kinsell et al 1953) suggests that the do employed in this trial has been inadequate Kinsell et advised the intravenous administration of corticotrop (20–40 units per litre) throughout the first three d of treatment, together with 200–600 mg of cortisone the oral or intramuscular route, daily 9 patients trea by this scheme of dosage obtained, without except significant decrease in proptosis within forty eight ho of commencement, an improvement maintained by c tinued treatment with corticotrophin gel These auth emphasised that very prolonged administration may required in some patients, and the high incidence untoward effects that attended such treatment is in sh contrast to the experience in this trial The conspicu therapeutic successes reported by Kinsell et al wo seem to require that a considerably higher dosage cortisone and corticotrophin be employed in any fu work (Dayton, Okie, and Beierwaltes 1954)

The best results in this series were obtained in those patients whose exophthalmos was of recent origin or had suddenly and rapidly progressed The most striking and constant clinical finding was the improvement in chemosis in each of the 15 cases where this feature was present

If local withdrawal of fluid from the orbital tissues and relief of orbital œdema were the factors responsible for clinical improvement (Campbell 1952) such an effect could only be expected in exophthalmos of recent origin before fibrotic changes have occurred in the ocular muscles and tissues Support for this hypothesis is afforded by the results of treatment seen in relation to the duration of history (table IV) for of 6 instances of exophthalmos of less than six months duration 3 showed improvement One of these (case 11b) had developed malignant exophthalmos after the incision of an abscess under general anæsthesia the rapid control of this patient's post anæsthetic increase in proptosis by corticotrophin was highly encouraging Of 23 patients in whom exophthalmos had been present for longer than six months only 5 obtained benefit from treatment

The patients in whom exophthalmos and thyrotoxicosis coexist form a group of particular therapeutic difficulty In this trial depression of thyroid function was observed in 8 of 15 patients initially thyrotoxic Of these, 4 derived some benefit from treatment regression of exophthalmos occurring concomitantly with apparent control of the thyrotoxic state 13 patients were euthyroid at the start of treatment and 4 of these obtained improvement in exophthalmos The difference in response between the two groups of thyrotoxic and euthyroid patients is not statistically significant but the depression of coexisting thyroid hyperfunction observed in some of the patients treated with cortisone or corticotrophin might perhaps suggest that these drugs are worthy of trial where thyrotoxicosis accompanies exophthalmos. There were however no specific features except perhaps chemosis which enabled a more confident selection to be made of suitable patients and further information and study are required here

The results in 10 patients who showed exophthalmos unaccompanied by ocular muscle weakness have been entirely disappointing and no benefit from treatment has been observed Most of these patients belonged to the group without chemosis and œdema

It is possible that the dietary restriction of sodium may be responsible for clinical improvement Of the 4 patients submitted to a low sodium intake 3 showed appreciable improvement

### Conclusions

1 No significant benefit occurred in the majority of patients suffering from exophthalmos and/or exophthalmic ophthalmoplegia from treatment with cortisone or corticotrophin (A C T H ) Inadequate therapeutic response may in some instances be referable to inadequate and insufficiently prolonged dosage

2 Cortisone and corticotrophin are worthy of further trial in patients with progressive exophthalmos of sudden or recent onset with chemosis

3 A group of patients whose proptosis was unaccompanied by chemosis and œdema and usually without ophthalmoplegia showed the least response to treatment

4 Coexisting thyrotoxicosis was reduced in a number of patients and half of these patients derived local benefit from treatment

5 If further trials are undertaken it is suggested that the dosage of cortisone and corticotrophin be considerably increased and special consideration be given to the use of serial intravenous corticotrophin infusions perhaps combined with dietary restriction of sodium

The panel wish to record the help given by Dr G N Chandler in the preparation of this report

*References at foot of next column*

# BRONCHOSCOPIC APPROACH FOR MEASURING PRESSURE IN LEFT AURICLE, PULMONARY ARTERY, AND AORTA

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SINCE the original papers were published on puncturing the left auricle through a bronchoscope (Facquet et al 1952 1954, Allison and Linden 1953) further experience of the method has been gained, a greater facility in the interpretation of the curves has been acquired and the technique has been extended to the measurement of pressure in the pulmonary artery and the aorta

With thoroughly effective local anæsthesia and smooth bronchoscopy puncture of the heart or of the great vessels is no more uncomfortable than simple bronchoscopy Such punctures were done on 121 patients without causing illness or death and 67 of them are reviewed here

### Method

*The apparatus* was similar to that previously described by Allison and Linden (1953) but was improved by the use of a shorter thicker walled wider bore Polythene tube which is now 25 cm long with 4 mm bore and wall 1 3 mm thick The resulting increased rigidity of the apparatus ensures a higher natural frequency of the recording system and prevents oscillation of the polythene tubing

*Puncture of left auricle*—When the bronchoscope is passed down the right side of the mouth it is usual to puncture the anterior wall of the left main bronchus 0 5–1 0 cm. below the carina Whichever side is used in the approach it is essential to direct the bronchoscope and needle along the line of the sternum When the pulmonary arteries are greatly enlarged the space between them at their origin may be so small that the left auricle is obscured , the arteries are then more liable to be pierced within the pericardium Although no obvious harm has resulted from this, at operation the pericardial fluid has been found stained for the large arteries are obviously more liable to bleed under increased tension When they are very large they may be avoided by passing the bronchoscope down the right main bronchus for 1–2 cm. to reach beyond the level of the arteries, and the auricle may then be reached by puncturing the anteromedial wall of the right bronchus

*Puncture of the pulmonary artery* is better done extrapericardially The bronchoscope is withdrawn into the trachea just above the carina the head of the patient is depressed further and the needle passes through the anterior wall of the trachea

*Puncture of aorta*—The aorta can be reached by inserting the needle 2–3 cm higher up the trachea than is done to reach the pulmonary artery

*Tracings*—In all the tracings an electrocardiogram and a phonocardiogram were recorded to facilitate the recognition of the individual waves of the pressure-pulse contours Pressure records were taken with the centre of the manometer membrane levelled to the manubrium

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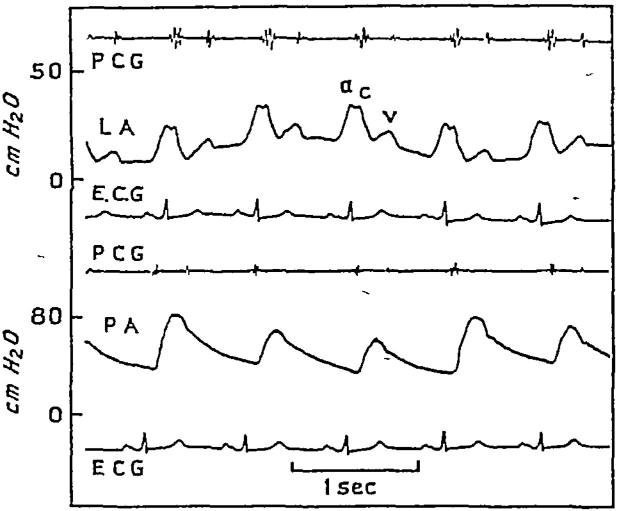


Fig 1—Typical record of pulmonary-artery (P A ) pressure, taken through bronchoscope immediately after recording left auricular (L.A ) pressure, in a patient with mitral stenosis and sinus rhythm P C G phonocardiograph

sternum, and this point is taken as the zero reference point in all the figures

## Results and Discussion

*Pulmonary Artery*

The pulmonary artery tracings, though valuable records, have not so far added anything to the knowledge gained from cardiac catheterisation To be able to take a record of pulmonary artery pressure and a left-auricular pressure at the same examination obviates the need for catheterisation and is particularly valuable for long-term follow up, for it can be repeated indefinitely A typical record of pulmonary artery pressure taken through the bronchoscope immediately after recording left auricular pressure is shown in fig 1

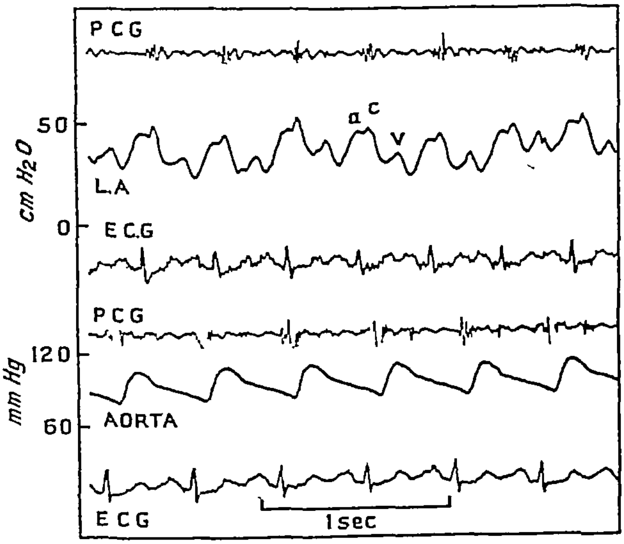


Fig 2—Left auricular (L.A.) and aortic pressures in a patient with mitral stenosis, showing absence of aortic incompetence.

*Aorta*

In some patients the aortic pressure was recorded, but the true value of this has not yet been assessed A bronchoscopic aortic pressure record is shown in fig 2 Clinically, the patient from whom this tracing was taken had mitral stenosis, and in addition the physical signs suggested either aortic or pulmonary incompetence The aortic record showed that there was no aortic incompetence

*Left Auricle*

The left auricular pressures in normal hearts i patients in this abnormal position and with a bronch scope in place were recorded in 5 patients with disea lung and no cardiovascular disease A typical exa of a left auricular pressure taken from a patient with normal heart is seen in fig 3 The *a* wave of systole is seen clearly starting 0 1 sec before the R of the electrocardiogram (E C G ) The *c* wave, in with the onset of ventricular contraction, is very and occurs 0 04 sec after the R wave It is notice mainly because of the abrupt alteration in gradient this point This is followed by the prominent *v* about 0 1 sec after the end of the T wave of the

61 patients with mitral disease, in whom the diagn was made with certainty, were included in this In 48 of them the diagnosis was confirmed at operat when examination of the external surface of the revealed the position of thrills, and a finger inside the auricle decided the presence or absence of a regu stream In the remaining 13 the diagnosis, determ on clinical and radiological evidence, was also be dispute but not confirmed by operation

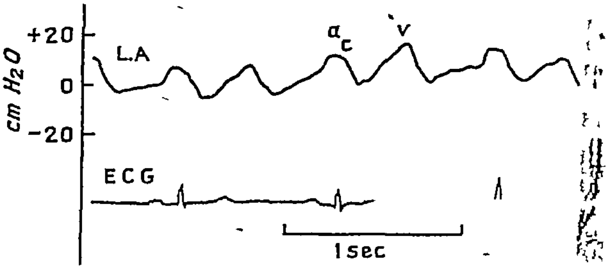


Fig 3—Left auricular pressure typical of normal heart.

The results fall naturally into two groups pa with sinus rhythm, and those with auricular fibrilla It is necessary only to attempt to differentiate betw mitral stenosis and mitral regurgitation within group

Of those with sinus rhythm 28 had pure mitral sten (26 confirmed at operation), and 6 were diagn clinically and radiologically as having mitral regu tion A typical record from a patient with pure stenosis is seen in fig 1 The appearance of the pulse contour is similar to that found in normal tra but the pressures at all points are raised The *a*, *c*, *v* waves are distinguished easily, and the magnitude the *v* wave is less than that of the *a* wave

The records from the 6 patients with sinus rhythm mitral regurgitation, though few, show different pres pulse contours They are similar to those obtained dogs by Wiggers and Feil (1922), who produced regu tation by preventing the mitral valve from closing d

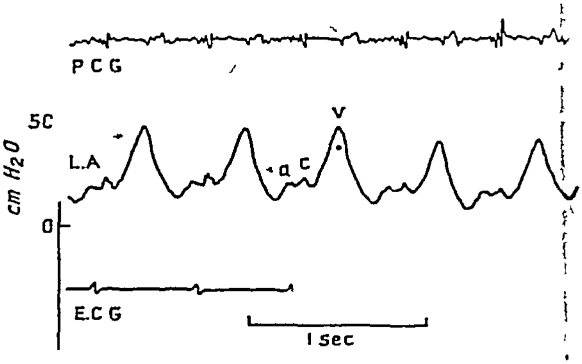
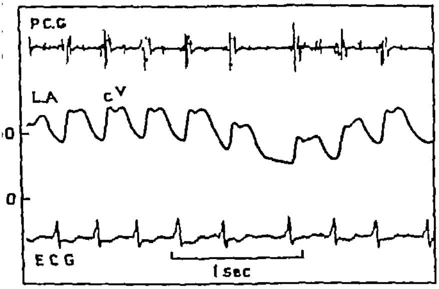


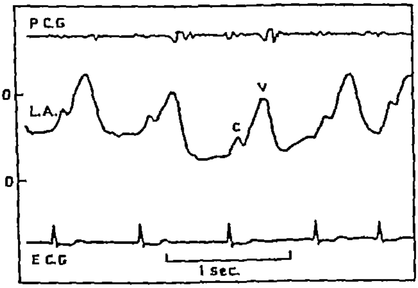
Fig 4—Left auricular pressure in a patient with mitral and sinus rhythm



g 5—Left-auricular pressure in a patient with mitral stenosis and auricular fibrillation.

ntricular systole. In these circumstances the left uricular pressure pulse contour showed a rise in pressure arting not in early systole but in mid to late systole ith a relatively high *v* wave. A record from a patient ith pure mitral regurgitation and sinus rhythm is seen fig 4 Again the three waves of the central venous ulse are seen clearly and there is a characteristic igh-climbing *v* wave

In patients with auricular fibrillation the auricular ontraction wave is absent, and each cardiac cycle begins ith an initial abrupt rise of pressure synchronous with e beginning of ventricular systole Records from 2 atients of whom one had auricular fibrillation and itral stenosis and the other auricular fibrillation and itral regurgitation are shown in figs 5 and 6 respectively These also show the increase in height of the *v* wave relative to the remainder of the pressure-pulse contour when a regurgitant stream is present



ig 6—Left-auricular pressure in a patient with mitral regurgitation and auricular fibrillation.

We do not claim that all cases may be divided strictly nto two groups those with stenosis and those with regurgitation because many patients have mixed lesions A record from such a patient, in sinus rhythm is seen in fig 7 On clinical and radiological findings this patient appeared to have pure mitral stenosis, but at operation there was a small regurgitant stream to be felt coming through the mitral valve. Although some regurgitation was suggested by the high *v* wave of the pressure pulse contour it was impossible to assess the degree However the occurrence of the mixed lesion of mitral stenosis and regurgitation appeared to be more common in the group with auricular fibrillation In accord with this Little (1951) thought that where the ventricular contraction is not immediately preceded by *an auricular contraction* regurgitation into the auricle always takes place However, it seems possible that this depends to some extent on the length of the previous diastole

In many patients with both stenosis and regurgitation the pressure tracing in the left auricle remains constant in successive cycles each wave form being a replica of the preceding one and a pattern for the one to follow, but occasionally, it seems regurgitation may occur in one cycle and not in another with the result that the wave contours vary Such a record is seen in fig 8 in which cycle 1 is typical of mitral stenosis whereas cycle 2 suggests regurgitation Closer examination shows that the left-auricular pressure-cycle 2 with the high-climbing *v* wave typical of mitral regurgitation is immediately preceded by a relatively long diastole and cycle 1 in keeping with mitral stenosis is preceded by a short diastole It seems that in this particular patient there was an appreciable regurgitation through the mitral valve during ventricular contraction when this followed a long diastole Wiggers and Feil (1922) produced evidence which supports this when they found that The regurgitation is definitely increased in slow beats Thus we infer that a patient with mitral stenosis may have an incompetent valve when the heart is beating slowly, though this may not be so when the heart is beating quickly Here is obviously a matter for further investigation

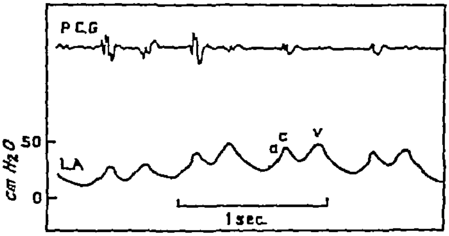


Fig. 7—Left-auricular pressures in a patient, with mitral stenosis and sinus rhythm in whom a small regurgitant stream was found at operation

After examination of the form of the tracings a quantitative study was attempted to see if a finer distinction could be made between stenosis and regurgitation Pressures were measured at two points the *z* point (Werle et al 1942) corresponding to the beginning of ventricular systole—i.e the beginning of the *c* wave—and the top of the *v* wave These were chosen because it was thought that the difference between them if great would indicate the presence of regurgitation for the auricular pressure in mitral incompetence rises during this interval The presence or absence of the

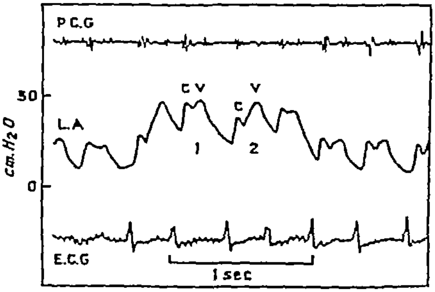


Fig 8—Left-auricular pressure in a patient with mitral stenosis and auricular fibrillation showing cardiac cycle 1 typical of mitral stenosis and cardiac cycle 2 typical of regurgitation.

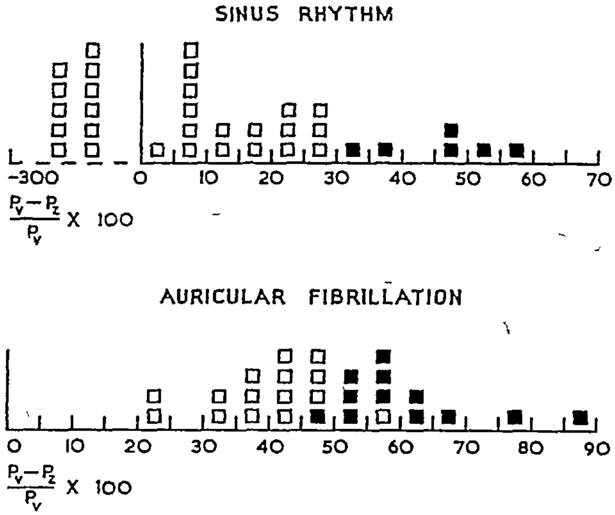


Fig 9—Analysis of left-auricular pressure-curves of 61 patients with mitral disease. Each open square represents a patient with stenosis, and each closed square a patient with regurgitation Along the abscissa are the left auricular mitral values derived from each patient s pressure-curve (explained in the text)

negative wave at this time was ignored, because it is considered to be due to dragging down of the valve ring by ventricular contraction

Many things affect the pressure in the left auricle, and, when all these are subject to variation from one patient to the next, it is difficult to assess the part played by any one of them in a group study With our manometers calibrated against an atmospheric zero levelled to the manubrium sterni it was obvious that respiration would affect the pulse contour, with the result that different points on the same cardiac cycle would be affected by different intrathoracic pressures To circumvent this difficulty all the measurements were taken from a cardiac cycle in an expiratory pause

Other factors affecting the pressure in the auricle are the volume of blood contained in the pulmonary vein-auricle system, the rate of flow of blood to the the volume-elasticity coefficient of the left auricle, an systemic arterial and left ventricular pressures F patient to patient these factors vary independentl the presence of regurgitation and would mask any att to indicate this regurgitation by the direct compa of records from different patients

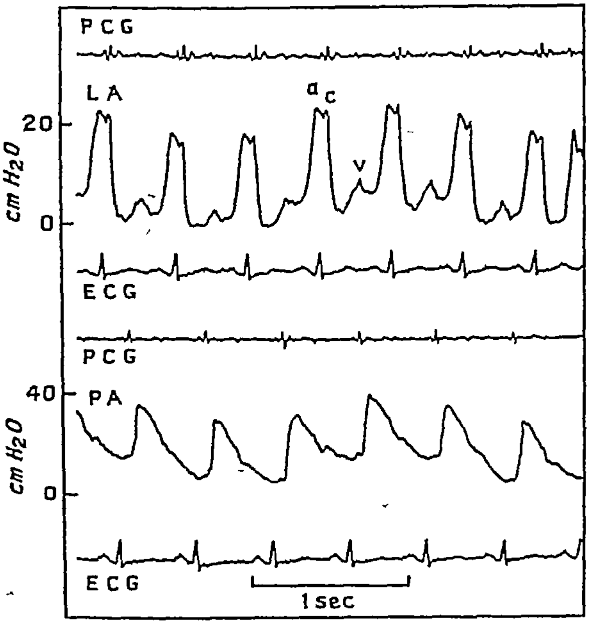


Fig 10—Left-auricular and pulmonary-artery pressures in a patient with mitral stenosis and neurosis, showing said pressures within normal limits

This difficulty has been largely overcome by the difference between the pressures measured at the of the $v$ wave and the $z$ point ($P_v - P_z$) as a of the pressure at the top of the $v$ wave ($P_v$) Thu obtain the expression $\frac{P_v - P_z}{P_v} \times 100$ This provide with a number which we have called the left-auri mitral value This is related to the pressures at and $z$ points but is little affected by the indiv patient variation which occurs in both numerator denominator and, to some extent, is cancelled out

The figure from this expression was worked out the left auricular pressure pulse curves of 61 p with mitral disease where the diagnosis was c determined

Fig 9 shows the results of this analysis In p with sinus rhythm, stenosis is clearly distinguished regurgitation by the left auricular mitral values In group with a left auricular mitral value of 25–30 patient (see fig 7) had a value of 29 and yet had a regurgitant stream at operation, being the only on this group to have any regurgitation at all

Fig 9 also shows the results from patients with disease and auricular fibrillation At first sight it app that the distinction between those with stenosis those with regurgitation, as one would expect, is clear-cut One patient, although having fibrillation a mitral value of 52, had a qualitative left- pressure-tracing like that of pure stenosis and had stenosis at operation Another patient, with fib who clinically and radiologically had mitral regurgi had a mitral value of 49, which indicated sten However, although the left-auricular pressure showed a rapid heart with the majority of cardiac c indicating mitral stenosis, an occasional longer dias was followed by a typical regurgitant curve It w indeed be surprising if there were a clear cut d between the two conditions, for many patients have stenosis and regurgitation

The above analysis is obviously very empirical spite of the attempt to justify it by simple mathem Many more patients must be examined before its v can be assessed Mitral regurgitation, when present, be diagnosed clinically and radiologically in most patie but in some there is uncertainty or a firm diagnosi subsequently found to be inaccurate It remains to seen if the method described above extends the po bilities of diagnosis into this latter group

That this simple technique is useful in assessing postoperative progress of patients after mitral valvoto is certain The patient whose symptoms recur may working too hard, he may have progressive pulmon vascular disease, or the valve may be narrowing ag Puncture of the left auricle is a quick and reliable wa deciding between these and other possible explanat for a raised pressure will surely indicate stenosis

A third use for this technique, not entirely separ from the above mentioned, is to help to differenti patients in whom the mitral lesion is not responsible all the symptoms A normal low left-auricular press is a contra indication to operation on the mitral va as in the following case

A married woman, aged 38, complained of a gripping c pain, breathlessness, dizziness, fainting attacks, and swell of the face, hands, and ankles The breathlessness was s to make it difficult for her to walk far and impossible to l

Specific therapy was withheld until *Sh sonnei* had been isolated from the stools. Treatment was considered to have been successful when the first six specimens taken after the end of treatment were negative for *Sh sonnei* and to have failed when *Sh sonnei* was isolated from any of these specimens. In each group the interval between the end of treatment and the sixth negative specimen averaged 9 days, with a range of 6–16 days in the tetracycline and streptomycin groups and 7–14 days in the phthalyl sulphathiazole group. All the follow-up specimens were taken while the patients were still in hospital.

### Bacteriological Methods

Fæcal specimens and occasionally rectal swabs were plated on to deoxycholate citrate agar directly (Hynes 1942) and after overnight incubation in selenite broth (Hobbs and Allison 1945). *Sh sonnei* was identified by colonial morphology on deoxycholate-citrate agar and by slide agglutination with S–R Sonne antiserum (Standards Laboratory).

Strains isolated from the tetracycline series were tested for sensitivity to tetracycline by a doubling dilution technique in tubes. A stock solution of 2500 µg per ml of tetracycline hydrochloride in distilled water was prepared each week and kept at 4°C. Further dilutions were made in a medium of the following composition:

TABLE II—DOSAGE OF TETRACYCLINE AND PHTHALYL SULPHATHIAZOLE

| Age (yr) | Tetracycline | | Phthalyl sulphathiazole | |
|---|---|---|---|---|
| | Regimen | Total dosage (g) | Regimen | Total dosage (g) |
| Less than 5 | 125 mg 6 hrly for 7 days | 3 5 | 0 5 g 6 hrly for 7 days | 11 |
| 5–15 | 250 mg 6 hrly for 7 days | 7·0 | 1 0 g 6 hrly for 7 days | 28 |
| More than 15 | 500 mg 6 hrly for 7 days | 14·0 | 2·0 g, 6-hrly for 7 days | 56 |

| | |
|---|---|
| Peptone | 2 0 g |
| Sodium chloride | 0 5 g |
| Glucose | 2 0 g |
| Distilled water | 100 ml |
| pH adjusted to | 7 6 |
| Andrade's indicator | 1·0 ml. |

A series of doubling dilutions of tetracycline in 1 ml volumes of this medium were prepared and 0 02 ml of a 1 in 100 dilution of a 24-hour broth culture of *Sh sonnei* was added to each tube. The sensitivity of the organism was taken to be the smallest final concentration of tetracycline that completely inhibited growth, judged by visible turbidity after 22–24 hours' incubation at 37°C. Strains isolated from the series treated with phthalyl sulphathiazole were tested for sensitivity to sulphathiazole by the disc technique described by Davies (1954).

### Results

The results of treatment are summarised in table III. Treatment was successful in 26 of the 27 patients treated with tetracycline, in 11 of the 32 treated with phthalyl sulphathiazole, and in 9 of the 25 treated with oral streptomycin.

TABLE III—RESULTS OF TREATMENT WITH TETRACYCLINE, PHTHALYL SULPHATHIAZOLE AND ORAL STREPTOMYCIN

| Result | Tetracycline | Phthalyl sulphathiazole | Oral streptomycin |
|---|---|---|---|
| Success | 26 (96%) | 11 (34%) | 9 (36%) |
| Failure | 1 (4%) | 21 (66%) | 16 (64%) |
| Total | 27 | 32 | 25 |

The strains isolated before treatment in 24 of the 27 cases treated with tetracycline were tested for sensitivity to tetracycline. All of them showed a uniform sensitivity to 4–8 µg of tetracycline per ml. All the strains isolated during treatment showed a similar sensitivity. The Oxford staphylococcus was sensitive to 0 5 µg of tetracycline per ml. A dosage of 0 5 g of tetracycline 6-hourly produced serum tetracycline levels of 4–5 µg per ml (Putnam et al 1953) and fæces tetracycline levels as high as 2230 µg per g of wet stool (Maynard et al 1953).

In the phthalyl sulphathiazole group 31 of 32 strains isolated before treatment were tested for sensitivity: fourteen were sensitive and seventeen resistant to sulphathiazole. Davies (1954) tested strains of *Sh sonnei* both by the disc technique and by inoculating about 150 viable organisms on to nutrient agar containing 5% lysed horse-blood and various concentrations of sulphathiazole. Strains recorded as sensitive by the disc technique were completely inhibited by sulphathiazole 1 mg per 100 ml by the other method; and strains resistant by the disc technique were not inhibited by sulphathiazole 50 mg per 100 ml.

The results of sensitivity tests with streptomycin are not given, because only a few strains were tested.

### Discussion

The number of patients, the age-distribution, and the interval between the onset of the disease and treatment were similar in each group. Although the tetracycline and the phthalyl sulphathiazole groups were strictly comparable, the streptomycin series differed slightly in that many of the patients were treated before March 1954. Successful results were obtained in only a third of the patients treated with phthalyl sulphathiazole or with oral streptomycin, whereas only 1 failure was recorded in the 27 cases treated with tetracycline. From this patient a scanty growth of *Sh sonnei* was obtained from a specimen taken on the second day after the end of treatment, but the following six specimens were negative without further treatment. However, in 1 case treated with tetracycline where twelve negative specimens were required before transfer to an institution a scanty growth of *Sh sonnei* was isolated from the twelfth specimen, although the preceding eleven were negative. This case has been classed as successfully treated because the first six specimens after the end of treatment were negative. In several of the patients treated with tetracycline the fæces were still positive on the 3rd and 4th days of treatment. We therefore feel that it would be unwise to reduce the duration of treatment to less than the 7 days that we have adopted. It is also possible that better results would have been obtained with oral streptomycin if the treatment had lasted longer. Most of our patients were given streptomycin for 3 days because this was the length of treatment used by Forbes (1953).

All the patients were nursed with full barrier technique, but reinfection may explain some of the failures (Vollum and Wylie 1946), though patients in all three groups were open to similar risks.

We found no toxic reactions to any of the drugs used. This confirms the low toxicity of tetracycline reported by Finland et al (1954), but the number of cases that we have treated is small and no special study of possible toxic effects was made.

Testing for sulphonamide sensitivity before treatment proved of little value in predicting the result of treatment with phthalyl sulphathiazole.

In 14 patients from whom sensitive strains were isolated before treatment there were 5 successes and 9 failures, compared with 5 successes and 12 failures in 17 patients from whom resistant strains were originally isolated. In 2 cases resistant strains were recovered after treatment although a sensitive strain had originally been isolated It is uncertain whether this was due to the development of resistance during sulphonamide therapy or to cross-infection The results of these sensitivity tests show that the failure of sulphonamide treatment in many of these cases cannot be attributed to sulphonamide resistant strains

### Conclusions and Summary

In a small trial we have compared the values of tetracycline, phthalyl sulphathiazole, and oral streptomycin in the treatment of Sonne dysentery Of 84 bacteriologically proved cases 27 were treated with tetracycline, 32 with phthalyl sulphathiazole, and 25 with oral streptomycin

Treatment was successful in only a third of the patients who were given phthalyl sulphathiazole or oral streptomycin, whereas there was only 1 failure with tetracycline Under the conditions of this investigation tetracycline proved superior to phthalyl sulphathiazole and oral streptomycin in effecting bacteriological cure

All the strains of *Sh sonnei* tested were sensitive to 4–8 µg of tetracycline per ml Sulphonamide sensitivity tests were of little value in predicting the results of treatment with phthalyl sulphathiazole

We thank Dr D C Liddle, physician superintendent, Monsall Hospital, and Dr M T Parker, director, Public Health Laboratory, Manchester, for their help and advice, and Dr A T. Mennie, medical director, Lederle Laboratories, for supplying the tetracycline ('Achromycin') used in this investigation

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# RELIEF OF PAIN IN INCURABLE CANCER

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THE purpose of this article is to describe new and wider applications of intrathecal therapy for relieving the pain of incurable cancer

Intrathecal therapy aims at selective cell destruction at the posterior root ganglia Introduced by Dogliotti (1931) for sciatic pain, and developed by Saltzstein (1934) and Stern (1934), it was applied with great success by Greenhill and Schmitz (1935, 1936) and Greenhill (1947) to pelvic carcinoma They used 0 75 ml of absolute alcohol, which floated *upwards* to the ganglia Complete relief of pain ensued in 60% of group III and IV cases, and partial relief in 10%

Last year it occurred to me that it would be an advantage to use a heavy "carrying solution," which could convey more than one destructive agent, thus increasing the therapeutic possibilities Moreover, a dense solution would be simpler to control—it is easier to lay a carpet than to paper a ceiling Phenol and silver nitrate were the agents I employed, with glycerin or propylene glycol as the vehicle

Injected intrathecally phenol can cause cord destruction (This was the subject of a recent case in law) If th [illegible] l is held in glycerin, however, its diffusion is at a minimum, and when injected intrathecally it falls downwards (sp gr of glycerin, 1 25, sp gr of cerebrospinal fluid, 1 007) With the patient on his side (as for lumbar puncture) it falls to the posterior root ganglia of his lower half (fig 1) Injected at the appropriate level it will usually cause permanent anæsthesia over the painful area Fig 2 shows the chief components influenced Motor units are not affected, their cell sta being well out of the way in the anterior horn Fu components affected lie in the posterior root

Fig 1—Radiograph after injection of ' (15 parts) and phenol (1 part) Resu anæsthesia over 1st, 2nd, and 3rd on inner side of arm, gave complete of pain

The aim is to select the group of smaller non-med C units of Erlanger et al (1926) The large A type proprioceptive units must be left intact This depend the concentration of the mixture, the optimum strength phenol in glycerin being 1 in 18 to 1 in 20 Such concentration appears to give the correct select affecting pain and touch fibres only, with loss of cutan sensation over the pain area—the only clear indicatio relief Cell selection in these circumstances is apparen on a size basis

### Agents and Procedure

0 2–0 3 ml of heavy cinchocaine hydrochloride ('Nu caine') (*the type used in spinal anæsthesia*) was employed a test agent

1 0–1 7 ml of 1 part of phenol in 18–20 parts of glyce well mixed with 0 1 ml of sterile water per ml, was agent used to provide permanent anæsthesia (If m water is added the phenol is activated and requires dilu to half)

1 ml of gr $^1/_{100}$ silver nitrate in glycerin was occasion employed when phenol proved inadequate

Largely for psychological reasons, the operation sho be carried out at the bedside For injection, the pat

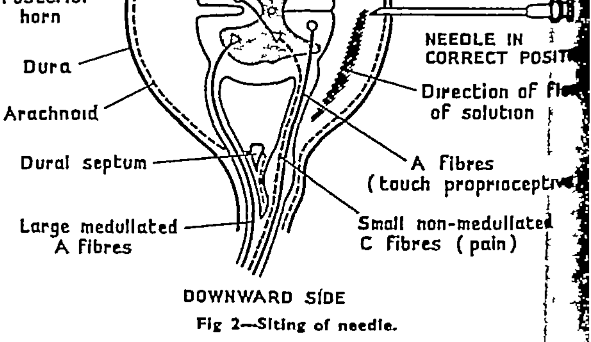

Fig 2—Siting of needle.

lies on his painful side in the lateral lumbar puncture position at the edge of the bed (fig 3A) Puncture is often best performed in the sitting position, and for injection the patient is carefully lowered on to his side. Sacral intrathecal injection is an exception the patient remaining seated for both puncture and injection

The needle is moved forward carefully millimetre by millimetre, and once cerebrospinal fluid appears the needle is advanced 1mm farther This prevents injection of the agent into the subdural space which might result from recession of the arachnoid following removal of C.S.F If the patient experiences bilateral ' root pain the needle has been inserted too far causing dragging of the nerve roots from touching the cord When C.S F flows, and before any injection is made the patient is rotated backwards so that the needle and syringe point upwards at an angle of 45° with the horizontal (fig 3B)

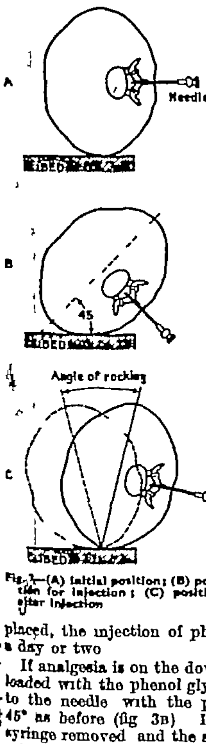

Fig. 3—(A) initial position; (B) position for injection; (C) position after injection

A preliminary test with nupercaine is made primarily to ensure that the needle is not directed upwards (fig 2 shows correct and incorrect positions) Using a 2 ml syringe 0 2–0 3 ml. of heavy nupercaine is slowly injected The patient is returned to the lateral lumbar puncture position, and rocked gently (fig 3C) Cutaneous sensory changes should appear on the patient's "lower" side sensory loss on the "upper" side means that the needle is directed too far upwards (fig 2) which would result in damage to the cord itself when the succeeding destructive agent is injected If the preliminary test shows that the needle is incorrectly placed, the injection of phenol should be postponed for a day or two

If analgesia is on the downward side the 2-ml syringe loaded with the phenol glycerin mixture is then applied to the needle with the patient rotated backwards at 45° as before (fig 3B) 1 3 ml is slowly injected, the syringe removed and the stylet inserted The patient is returned to the normal lateral lumbar puncture position and gently rotated backwards and forwards through this angle (fig 3C) Sensation must be tested immediately and if sensory loss is extending too far caudally the foot of the bed should immediately be held upwards by assistants to let the solution flow towards the cephalic end Conversely the head of the bed should be held up if sensory loss is spreading too high A further 0 5 ml of phenol mixture can be added if necessary

After the phenol has been injected the needle is left in situ for one hour If sensation returns even in the form of analgesia, pain will almost certainly also return before long In such circumstances the injection of gr $^{1}/_{100}$ silver nitrate dissolved in 1 ml. of glycerin, may successfully produce more permanent anaesthesia Intensification is obtained by adding 1 in 500 000 methyl sulphonal The effect of adding hyaluronidase is being investigated.

At the end of the procedure the patient can be gradually raised Plenty of fluids should be given and sedatives as required

Anæsthesia is at first widespread. In lumbar injections it often extends initially from lower abdomen to ankle but settles later to an area from groin to upper tibia It should overlap the pain area considerably If the anæsthesia is still present at the end of five days its effect is probably permanent and the patient should be allowed to go home but if necessary the phenol injection can be repeated after a few days

## Site of Injection

### *Pain of Pelvic Origin*

(*a*) Obturator and femoral distribution (groin, knee and thigh) Injection is made in the twelfth dorsal and first lumbar interspaces.

(*b*) Sciatic type Injection is made in the second or third lumbar interspace and the solution allowed to flow caudally by slight elevation of the head of the bed.

(*c*) Sacral pain (carcinoma of rectum) Injection is made in the fifth lumbar and first sacral interspaces with the patient sitting upright on a pillow and held backwards by assistants. A second or two after injection he is pulled forwards so that the solution can reach the lower sacral roots in the tip of the dural sac S 3 2 and 1 units can be covered in cases of lower sciatic involvement if when the tip of the dural sac is filled the patient is rotated on to his side quickly

### *Abdominal Pain from Carcinoma of Stomach Pancreas, &c*

Injection is made at the appropriate level—often sixth or seventh dorsal interspace—and repeated after a few days on the other side

### *Carcinoma of Lung*

Injection is made at a level corresponding to the pain and often at segments above and below

### *Brachial and Cervical Pain from Primary or Secondary Carcinoma*

Injection is at the fourth or fifth cervical interspace and the solution is allowed to flow caudally by gently raising the head of the bed. Alternatively it may be made at the second thoracic interspace and the solution allowed to flow in the opposite direction with the patient's head itself elevated as much as possible

After-effects are usually mild at most they consist of headache and vomiting which pass off in a few hours Brief aching in the affected area usually indicates success Paresis of the leg occurred in 3 out of 22 pelvic cases and was due largely to inexperience with the strength of the solution Urinary incontinence was a temporary complication in the rectal group Bedsores and burning have to be guarded against and the patient should as far as possible always lie on the sound side

## Results

The regions affected in the 37 patients treated with intrathecal injections of phenol were cervix (15 patients) rectum (5) genito urinary tract (2) stomach (2) brachial and cervical region (6) and lung (7) Results were based on the patients own statements on clinical observation, and on the reductions which it was subsequently possible to make in the dose of their analgesic drugs Of 19 successes now deceased 6 obtained almost complete relief right up to the time of death. The remainder were relieved to within a few days of their death The duration of relief varies 1 case of carcinoma of the rectum obtained seven months relief and several have been relieved for six months 8 of the 37 were apparently unrelieved ; 4 had carcinoma of the cervix 3 carcinoma of the bronchi and 1 carcinoma of the stomach

### Advantages

(1) The method is simple, and with care it can be carried out in any hospital For the patient it is a minor procedure

(2) A series of ganglia can be influenced by increasing the quantity of phenol injected, and by tilting the patient 3 patients were successfully given additional injections for involvement of new areas

(3) Alternative sites of injection can be used—e g, fourth and fifth cervical or second thoracic interspace, depending on whether the head or the foot of the bed is raised

(4) It can be used for cervical, dorsal, lumbar, or sacral units

(5) The method is safe, paresis, at the 1 in 18 strength, was slight On the other hand, retention often lasted three weeks in rectal cases

### Conclusion

At the time of injection the criterion for relief was a fixed anæsthesia over the pain area On this basis the cases were of two types

*Single nerve groups affected* (e g, obturator, sacral, or sciatic)

*Combined nerve groups affected* (e g, obturator plus sacral or obturator plus sciatic, and some cases of carcinoma of lung)

In the first type the pain was easily relieved In the second, however, it proved intractable Even with nupercaine the anæsthesia was either fleeting or entirely absent All were cases of advanced carcinoma, and in 6 the spine was involved. At necropsy 4 showed infiltration of the dura phenol could not reach the carcinoma encoated ganglia in these cases, but it did cause temporary anæsthesia of the emerging roots Thus the hypothesis of pain from perineural lymphatic invasion (Way 1951) might also apply to the ganglia and dura For uniform success, therefore, and since most cases follow the same pattern, a wide ganglion block should be carried out in the early stages of pain, before the growth has involved the ganglia

Finally, in three extreme cases of very advanced carcinoma "released phenol," made by adding 0 4 ml sterile water to 0 5 ml of 1 in 30 phenol in glycerin, was used, and produced anæsthesia from waist to feet Paralysis ensued in 1 case Further research is proceeding on the possibility of producing selective spinal cord block without causing motor weakness

### Summary

37 cases of incurable cancer were treated by intrathecal phenol Relief of pain was obtained in 29 cases

Success apparently depended on whether single or combined nerve groups were involved

Phenol in glycerin or propylene glycol was used with success at all spinal levels, including the cervical region

The immediate aim was to produce fixed skin anæsthesia over the painful area

Spinal cord block was attempted in 3 instances, and gave relief

My thanks are due to Dr Ralston Paterson (director) and Dr E C Easson, of the Christie Hospital and Holt Radium Institute, for referring patients to me, and to Dr and Mrs J Starkie and Mr F Young for their invaluable help

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# CYCLOPROPANE, DENTAL EXTRACTION, AND SPARKS

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THAT sparks might be thrown off when a forceps fractures the enamel of a tooth during its extraction was not foreseen when cyclopropane as an alternative to nitrous oxide anæsthesia was advocated by one of us (Bourne 1952, 1954a) Ignorance of this possibility seems to have been shared by others, and incredulity was expressed (Henry 1954) when Newton-Andrews (1954) reported that, while giving nitrous oxide, he had seen "a shower of sparks" plainly visible in a well-lighted surgery

Though this occurrence may have been singular it contra indicated the use of cyclopropane anæsthesia for dental extraction until the matter had been investigated (Bourne 1954b) The advantages of this method of anæsthesia and its successful trial over a period of years on more than 2000 patients prompted us to undertake such an investigation We report here our investigation and suggest a simple safeguard

### Method

" Enamel, the hardest substance produced in the body sparks with steel like flint" (Cowdry 1944) This fact can be easily demonstrated We have obtained sparks, visible in daylight, by the application of dental forceps, made either of stainless or plated steel, to the crowns of extracted teeth, whether deciduous or permanent, whether molar, premolar, canine, or incisor, whether healthy or cavitated, whether filled or unfilled, and whether dry or wet with saliva and blood (After a few applications the plating becomes erased from the biting surface of plated forceps, exposing the steel )

The best display of sparks was obtained when fine root forceps were strongly applied to the crowns of healthy molar teeth and then were made to fracture the enamel Though this manœuvre would seldom, if ever, be used in clinical practice it was the one used in experiments 1 and 2 (fig 1)

*Experiment 1 Influence of Oxygen on Sparking*

In an atmosphere of carbon dioxide (which does not support combustion) sparks, viewed in the dark, appeared only as the slightest local redness Occasionally a dull red particle was thrown off about an inch In air (21% oxygen) the sparks were orange red and were often seen to fly a foot or more When oxygen was added to air, the number and brilliance of the sparks increased In pure oxygen a shower of white sparks was obtained at almost every trial and with the greatest ease

*Experiment 2 Influence of Oxygen on Ignition*

In this experiment we tested the ability of sparks produced with forceps and teeth to ignite various mixtures of cyclopropane, oxygen and nitrogen passing through a semitransparent rubber tube The apparatus used is shown in fig 1 The gas flows were measured by rotameters, checked, and, where necessary, recalibrated with a Parkinson and Cowan gas meter The composition of the resulting mixtures was further confirmed by analysis by the method referred to below

The tooth and forceps were manipulated by hand through the rubber (fig 1) Owing to the imperfect transparency of this rubber only bright sparks were visible, even in the dark. These alone were taken into account in the results shown in the accompanying table With the lower proportions of oxygen the cyclopropane concentration was adjusted to give mixtures which, according to Guest et al (1952), were most easily ignited by an electric spark The inflammability of each mixture that failed to be ignited by sparks from teeth

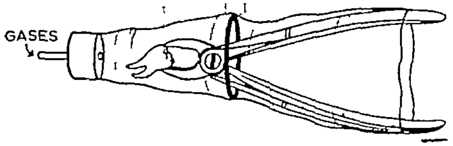

Fig 1—Apparatus for testing ignition of gas mixtures by sparks produced with dental forceps and teeth. The gases comprising the mixtures were led to the apparatus through separate tubes.

and forceps was confirmed by igniting it with an induction coil spark from electrodes passed into the apparatus

*Experiment 3 Ignition with Sparks from Dental Forceps and Grindstone*

A dental forceps applied to a grindstone driven at high speed by an electric motor gives off a stream of sparks apparently in every respect far in excess of any that can be obtained with teeth As expected this was found to be a more effective means of ignition than was striking sparks with teeth. In this experiment the same apparatus was used as in experiment 2 except that the forceps and tooth were dispensed with and the end of the tubing which in experiment 2 gripped the forceps handles, was now held open The stream of grindstone sparks, directed through the opening passed down the tubing to the end at which the gases were being delivered

With this arrangement the mixtures listed in the table down to and including that which contained 28% oxygen were ignited at once The mixture, however which contained 25% oxygen, and other mixtures, not listed, with still less oxygen could not be ignited. Nor with 25% oxygen, could mixtures in which the cyclopropane concentration was varied throughout the whole of its ignitable range be ignited by this method though all of them were instantly ignited, during each test, by induction-coil sparks.

*Experiment 4 Ignition of Cyclopropane in Nitrous Oxide*

Using the grindstone method we were able to ignite a mixture consisting of 10% cyclopropane and 90% nitrous oxide 10% cyclopropane in other mixtures in which oxygen was added at the expense of nitrous oxide were also ignited.

INFLUENCE OF OXYGEN ON IGNITION OF CYCLOPROPANE BY SPARKS FROM TEETH AND FORCEPS

| Cyclopropane (%) | Oxygen (%) | Nitrogen (%) | Ignited by sparks from teeth and forceps | No of times sparks seen before ignition |
|---|---|---|---|---|
| 20 | 80 | | Yes | 0 |
| 35 | 65 | | Yes | 0 |
| 45 | 55 | | Yes | 9 |
| 15 | 60 | 25 | Yes | 4 |
| 16 | 40 | 44 | Yes | 50 |
| 9 | 34 | 57 | Yes | 10 |
| 8 | 30 | 62 | Not with 100 sparks | |
| 8 | 28 | 61 | (Not tested) | - |
| 8 | 25 | 67 | Not with 100 sparks | |

*Experiment 5 Ignition of Ether and Divinyl Ether (Vinesthene)*

The vapour of each of these agents in oxygen was ignited with the greatest of ease by sparks from teeth A mixture containing nitrous oxide and oxygen at flow rates of 6 litres and 2 litres respectively which had passed over ether in a bottle was ignited at once by grindstone sparks.

The results of our first three experiments suggested that should sparks such as we have produced experimentally be formed during the extraction of teeth when cyclopropane had been administered, the likelihood of an explosion resulting would depend mainly on the concentration of oxygen present in the mouth at the time To carry the investigation further therefore it was necessary to anæsthetise patients by the method under review and to measure the proportion of oxygen in the exhaled gases This method of anæsthesia described by Bourne (1954a) is as follows

A rubber bag of about 6 litres capacity is filled with cyclopropane and oxygen in equal parts. The bag is connected to a face piece by a two-way stopcock The stopcock shuts off the bag and leaves open an aperture through which air is breathed while the face piece is being adjusted over the patient's mouth and nose When this has been done the stopcock is turned, closing the air aperture and allowing the patient to breathe in and out of the bag At the end of the administration the whole apparatus is removed from the face and the extractions are undertaken

It was recommended by Bourne that the administration should be continued for about a minute but since we found that the amount of oxygen in patients' exhalations increased a little when the administration was prolonged in the 13 patients we have examined we continued it for two or three minutes so that the oxygen would reach the highest levels possible

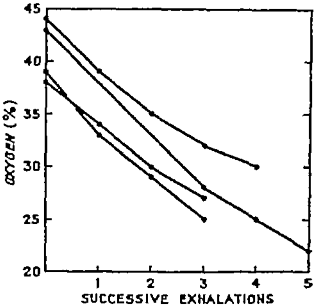

Fig. 2—Concentration of oxygen in successive exhalations of 4 patients breathing air after withdrawal of anæsthetic mixture (cyclopropane 50% with oxygen 50%)

From this description it will be realised that with this method of anæsthesia sparks could be struck only after the anæsthetic had been withdrawn and only during an exhalation might the patient be in danger from an explosion due to this cause We therefore analysed exhalations for their oxygen content

### Measurement of Oxygen in Patient's Exhalations

The samples of exhalations were drawn into syringes through needles passed through a rubber diaphragm in a specially prepared face piece The first sample was taken just before the end of the administration At the end of the administration the anæsthetic was withdrawn by turning back the stopcock so that the bag was shut off The patient then breathed air through the aperture while the face piece was retained on his face In this way we were able to continue to sample the exhalations from under the face piece after known numbers of inhalations of air

*Cyclopropane 50% with Oxygen 50%*

Of the 13 patients examined 7 were children, the youngest being aged 3 years The oldest adult was aged 82 Since in clinical work some error in adjusting the flow rates of the gases occurred the contents of the bag were analysed before each administration It was found that the oxygen varied between 40% and 54% The results of this experiment are presented in fig 2, which shows the values we obtained in 4 of these patients including the 1 who gave the highest values Usually as expected higher values were found in children than in adults.

*Cyclopropane 50% with Oxygen 25% and Nitrogen 25%*

A further series of 13 patients were anæsthetised in exactly the same way as those in the foregoing experiment and just before the anæsthetic was withdrawn their exhalations were sampled In these patients, however 50% cyclopropane was administered not with oxygen but with oxygen and nitrogen in equal parts delivered from a cylinder containing the mixture (At flow rates of 750–1500 c.cm per minute the oxygen nitrogen mixture can be measured with sufficient accuracy through an oxygen rotameter ) As in the previous experiment and for the reason there given the contents of the bag were analysed shortly before each administration On one occasion they were found to consist of 42% cyclopropane and 29% each of oxygen and nitrogen The oxygen in fact varied between 25% and 29%. We found that in none of these patients did the oxygen concentration in any exhalation rise above 23%

*Analysis of Samples of Gas* ,

The gases were analysed by a method based on Guthrie's (1921) apparatus for the analysis of air The samples were passed directly into the capillary tubes of each of three absorbing vessels in series The first contained concentrated sulphuric acid, the second sodium hydroxide, and the third an oxygen absorbing solution These absorbed cyclopropane, carbon dioxide, and oxygen in turn As a measure of the accuracy of this method 10 analyses of air gave a mean oxygen percentage of 20 5% with a range of ±0 5%

## Discussion

The energy required to ignite cyclopropane oxygen nitrogen mixtures is inversely proportional to the concentration of oxygen and directly proportional to that of nitrogen This has been shown precisely by Guest et al (1952) using electrical energy Our findings with sparks from forceps showed a similar trend Furthermore, it seems probable from experiment 2 that the effectiveness of sparks from forceps, considered as a source of ignition, decreases with decreasing oxygen If this is so, there are two influences both of which (should sparks be formed during the extraction of teeth) would make an explosion less likely when the oxygen is low than when it is high

From our experiments we feel justified in concluding that the ignition of cyclopropane by sparks produced with forceps and teeth during extractions is unlikely when the concentration of oxygen in the mouth does not exceed 30%, and is improbable in the extreme when the concentration is 25% or lower

The oxygen concentration in the exhalations of patients anæsthetised with 50% cyclopropane with 50% oxygen decreased to 25% only after a few breaths of air had been taken During these few breaths, therefore, it would be wise to consider patients at risk from an explosion

It might be thought that this danger could be avoided by asking the dental surgeon to wait until these breaths had been taken But in our view this could not be relied on, since dental surgeons are wont not to pause at this stage Or, again, it might be thought that the formation, during an extraction in normal clinical practice, of the sparks reported by Newton-Andrews (1954) was unique, and therefore this danger could be altogether ignored Certainly the manœuvres we used to produce sparks experimentally were quite unlike any that might be used in practice Nevertheless we believe that, under certain conditions, sparks could be produced During the extraction, for example, of an upper molar tooth with a cervical cavity on the lingual side and with buccal and palatine roots inclined steeply away from one another, forceps tend to slip downwards towards the crown and may fracture the edge of the cavity After several trials with extracted teeth we produced sparks in this way We have produced sparks also when teeth simply broke, an accident which we have often seen in practice Moreover, though sparks formed in clinical practice have not, so far as we are aware, been reported before the communication of Newton Andrews, possibly they may have been produced but went unnoticed under normal lighting conditions On the other hand, it might be argued that the risk is no less with ether or divinyl ether given with a large concentration of oxygen—a practice that, with divinyl ether at any rate, has been current for many years without, so far as we know, there having been reported an explosion caused in this way

We conclude that, when cyclopropane, divinyl ether, or ether is administered with a large concentration of oxygen, the patient is momentarily at risk if extractions are made immediately after the mask has been removed We th[illegible]re suggest that cyclopropane should be used n[illegible]gen but with a mixture of oxygen and nitrogen in equal parts Cylinders of this oxygen-nitrogen mixture for medical use are readily available commercially We have administered 50% cyclopropane with this oxygen-nitrogen mixture with results that were clinically indistinguishable from those we obtained when 50% cyclopropane was used with 50% oxygen In 13 patients examined the concentration of oxygen in the exhalations did not then increase above 23%

In conclusion, though detailed comment is outside the scope of this report, we draw attention to the fact that, when inflammable agents are used, the hazard we have investigated is probably, in any case, smaller than that from static sparks Needless to say, therefore, precautions, which are now well known, should always be taken to avoid this latter danger

## Summary

Enamel, the hardest substance in the body, like flint, gives sparks with steel

Experimentally we have produced sparks, visible in daylight, with teeth and dental forceps

The number and brilliance of these sparks increased with increasing oxygen in the surrounding atmosphere.

With these sparks we ignited cyclopropane in oxygen With decreasing concentrations of oxygen ignition became increasingly difficult When the concentration of oxygen was as low as 30% we failed in a hundred consecutive attempts, at each of which good sparks were seen

With sparks from teeth and dental forceps we ignited with great ease the vapour both of ether and of divinyl ether in oxygen

A grindstone applied to dental forceps threw off a stream of sparks far in excess of any that could be obtained with teeth With these sparks we ignited cyclopropane oxygen-nitrogen mixtures with concentrations of oxygen as low as 28% but failed to ignite cyclopropane throughout its entire inflammable range with concentrations of oxygen that were 25% or less

We concluded that, when cyclopropane is used, patients should be considered to be at risk from an explosion due to sparks from dental forceps and teeth if the oxygen in their exhalations exceeds 25%

The concentration of oxygen in the exhalations of 13 patients anæsthetised with 50% cyclopropane in 50% oxygen by the method described by Bourne (1954a) was measured It did not decrease to 25% until several breaths of air had been taken

We suggest that, as a safeguard, 50% cyclopropane should be administered not with oxygen but with oxygen and nitrogen delivered from a cylinder containing these two gases mixed in equal parts Such cylinders for medical use can be readily obtained commercially The flow rate of the oxygen nitrogen mixture can be measured with sufficient accuracy with an oxygen rotameter

With this mixture anæsthesia was clinically indistinguishable from that which we obtained when cyclopropane was used with 50% oxygen, and in 13 patients examined the concentration of oxygen in the exhalations did not increase above 23%

We wish to thank Miss I M Young, lecturer in physiology, Sherrington School of Physiology, St Thomas's Hospital, and Mr N Thurlow, senior technician there, for suggesting the method of gas analysis and for their helpful advice in its use

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# PREFRONTAL LEUCOTOMY
## A CLINICOPATHOLOGICAL REPORT

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FOR most of the mentally ill patients who come into the neurosurgeons hands a restricted leucotomy or topectomy is now the operation of choice

Clearly preferences for different forms of leucotomy should ultimately depend on a large series of detailed clinicopathological correlations but not enough of such material is available. In these circumstances the publication of a single clinicopathological study is justified Not only will it make a small contribution to the evidence available for a later analysis but the difficulties of interpretation which become apparent when the clinicopathological correlations are discussed may usefully draw attention to those deficiencies in our present knowledge which most require investigation

Careful analysis of published cases does not provide evidence sufficient to sustain the widespread and enthusiastic belief that a bimedial inferior cut is always the modified operation of choice In this operation the section of the white fibres is in the usual plane but is limited as far as possible to the ventromedial quadrant of each lobe It is sometimes called an orbital leucotomy Further in the present case full recovery from a *non-psychotic* mental illness followed a leucotomy in which these ventromedial segments virtually escaped damage The clinical findings suggest that the improvement in this patient depended on personality changes These were of a type which, in other patients might bear no causal relationship to therapeutic success In such patients they would be an irrelevant defect in the present case, it is argued they were essential to recovery

### Case report

A married woman aged 59 diagnosed as suffering from (i) tinnitus due to middle-ear disease, and (ii) a hypochondriasis with hysterical features, complained mainly of terrible head noises, palpitation, and weakness of the legs.

*Family History*—Her father was an alcoholic who terrorised the family while in his cups The only other child her elder brother was described as obsessional and eccentric. He was discharged from the Navy with neurasthenia and has at times drunk to excess. She had one adult daughter who like the patient s mother was not known to be abnormal

*Personal History*—At the age of 4 she had measles followed by double pneumonia Subsequently she was a fragile nervous, and sensitive girl who was terrified of her father s alcoholic bouts For 12 years she worked as a lady s maid and at the age of 30 she married her childhood sweetheart a chauffeur Her married life had been happy After the birth of her daughter she underwent appendicectomy and nephropexy Otherwise she had been well

*Personality*—The patient described herself as always rather pessimistic but her husband characterised her as " rather a spark and it seemed that she had been capable and hard working but nevertheless full of life and gaiety Although an extremely active woman who was always bottling preserving and knitting she was inclined to be excessively anxious over small matters and would arrive over early for trains. She was meticulous with her clothes and fussy about the house and would get upset if her routine were put out Liable to headaches she was careful of her health. She had few interests outside her home and family and her friends were chiefly those of her youth Gardening singing and sketching were her hobbies

*Present Illness*—At the age of 25 an attack of flu left her with a ringing noise in the head mainly in the left ear This noise gradually lost its intensity and after a time became so faint that she could only hear it if she especially listened for it. 27 years later at the age of 52 she had an attack of gastric flu with diarrhœa and vomiting and after this the noises increased in intensity They became worse and 4 years later were intolerable

*On admission* she described them as varying—sometimes like the reverberations of beaten iron, at others like clanging cymbals or the dragging of heavy chains. Often the noises were so loud that she could feel something hitting the inside of her head which at times seemed to be jerked about For a year or two she had felt weak, lifeless, and depressed with the result that she could not attend to her normal household duties. Her legs were weak and tremulous Palpitations were accompanied by a dreadful pain in the chest Although she was constipated her appetite remained good

*On examination* she was well nourished neat and self composed She told her story with a wealth of circumstantial detail and the house-officer noted that her mood was characterised by complacency rather than severe depression or emotional distress Physically apart from a chronic lesion of the right inner ear there was no evidence of organic disease of the nervous system She had hypertension (blood pressure 250/130 mm Hg) and arteriosclerosis.

*Operation*—On Nov 12 1948 Mr Harvey Jackson carried out a standard prefrontal leucotomy

*Postoperative State*—Immediately after the operation the patient was grossly confused. She had urgency and incontinence Her confusional state resolved rapidly and after a short convalescence she returned home much less worried by her noises but distinctly apathetic

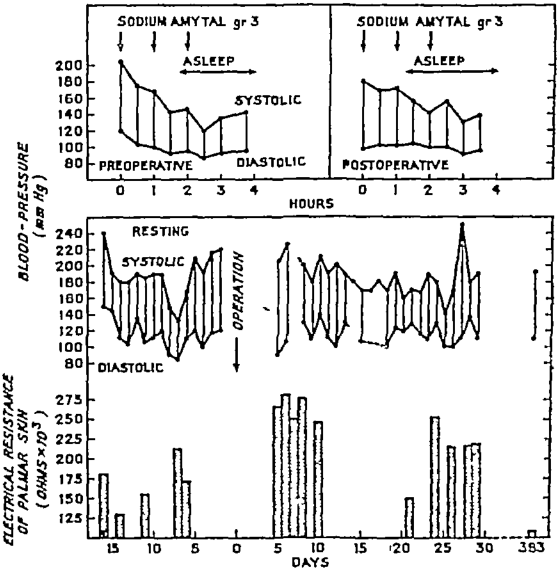

Fig 1—Blood-pressure at rest and under sodium-amytal sedation and electrical resistance of palmar skin before and after leucotomy

*Follow-up*—3 months after the operation a home visit disclosed that she was more alive and interested She was using make up again and planning her future wardrobe in a sensible manner Only once had she been incontinent, but she had been troubled by some urgency Her husband and her daughter were both very pleased with her progress, finding her unworried and placid but very lazy She was helping little with household tasks and mostly sat about doing nothing She had done some shopping in a competent manner, but she herself noticed that she was 'slower on the uptake," and her daughter found her distinctly forgetful Her appetite was excessive A year after the operation her husband reported that she was still improving She concentrated better and was taking the initiative in such matters as altering her own clothes and mending her husband's Her cooking was good but plainer, and she still occasionally forgot to put salt in the potatoes She found it difficult, moreover, if she was put out of her routine—e g , if someone extra came to a meal, or if her daughter tried to persuade her to try a new recipe She enjoyed going out more than she had done for the past 6 or 7 years, but in the cinema she became lost if the plot was complex Of her tinnitus she said "I have those noises but I can't be bothered with them" Her husband thought that her personality was improved and she was not an invalid in any way "If she could sleep more and eat less, she would be no problem at all" 6 months later she was still happy go lucky, did not appear to bother about anything, and when warned by her husband about leaving her bag in the shops she replied "If I lose it I lose it" In June, 1950, she had what was probably a small cerebrovascular accident, which was followed by an increase in her apathy and a further impairment of her powers of memory and concentration In December, 1952, she died of cardiac rupture

*Electro encephalography*—Before the operation the electro encephalogram was symmetrical, with a normal alpha rhythm The record was dominated by a generalised high voltage rhythm of 20 cycles per sec Twenty days after the operation distinct changes were observed The alpha rhythm at 10–11 cycles per sec was of greater amplitude and spread further forward The fast rhythm of 20 cycles per sec was no longer apparent but may have been masked Irregular slow activity of 1–3 cycles per sec was seen bilaterally in the prefrontal regions but was much more extensive on the right, where it was seen as a focus A year after the operation the only abnormality was a small amount of low voltage slow activity in the frontal regions, now greater on the left than on the right 4 years after the operation (Nov 6, 1952) the frontal slow activity was only just discernible, but the record showed a new abnormality a bilateral theta rhythm at about 7–8 cycles per sec predominantly in the left frontotemporal area There were also, on over breathing, suggestions of spikes in the left frontotemporal region

*Psychological Tests*—The patient was tested with the Wechsler Bellevue scale before the operation and 1 4, 10 and 48 months after it She scored an intelligence quotient of 110 before the operation and her results showed no significant evidence of intellectual deterioration A month after the operation there was clear evidence of intellectual impairment Her scores on all subtests except picture completion, similarities, and block design showed not only no practice effect but even a definite loss T[illegible] was most evident on the pic[illegible]ement, digit span, and digit symbol substitution subtests 3 months later her performance had definitely improved, but 19 months after the operation it was still below her preoperative level 4 years after the operation there was evidence that further deterioration had taken place Her performance on all subtests was consistently below what it had been before the operation she could not reproduce the Terman designs, her performance at Weigl's sorting test was poor, and she failed to learn the Babcock sentence after nine attempts

*Autonomic Functions*—On admission her blood pressure was 250/130 mm. Hg Her *urine* was normal, *blood-urea* 40 mg per 100 ml , and *urea clearance* 102% *Intravenous pyelography* revealed no functional or anatomical abnormality Her *heart* showed some left ventricular enlargement The blood pressure was recorded morning and evening in the right arm Though the evening values tended to be higher than the morning values, leucotomy affected both in a similar manner, and only the evening values are presented here (fig 1) It will be seen that there was no pronounced fall in either the systolic or diastolic pressures even in the immediate postoperative period A year after the operation (Nov 30, 1949) the patient's blood pressure was recorded in the outpatient department It was then 220/125 mm Hg After 15 minutes' rest the mean of three readings was 192/112 mm. Hg In November, 1952, the blood pressure was 230/125 mm. Hg These values were essentially the same as those found preoperatively In addition to the resting blood pressure observations 'Sodium amytal' sedation tests were done both before and after operation The results of these are given

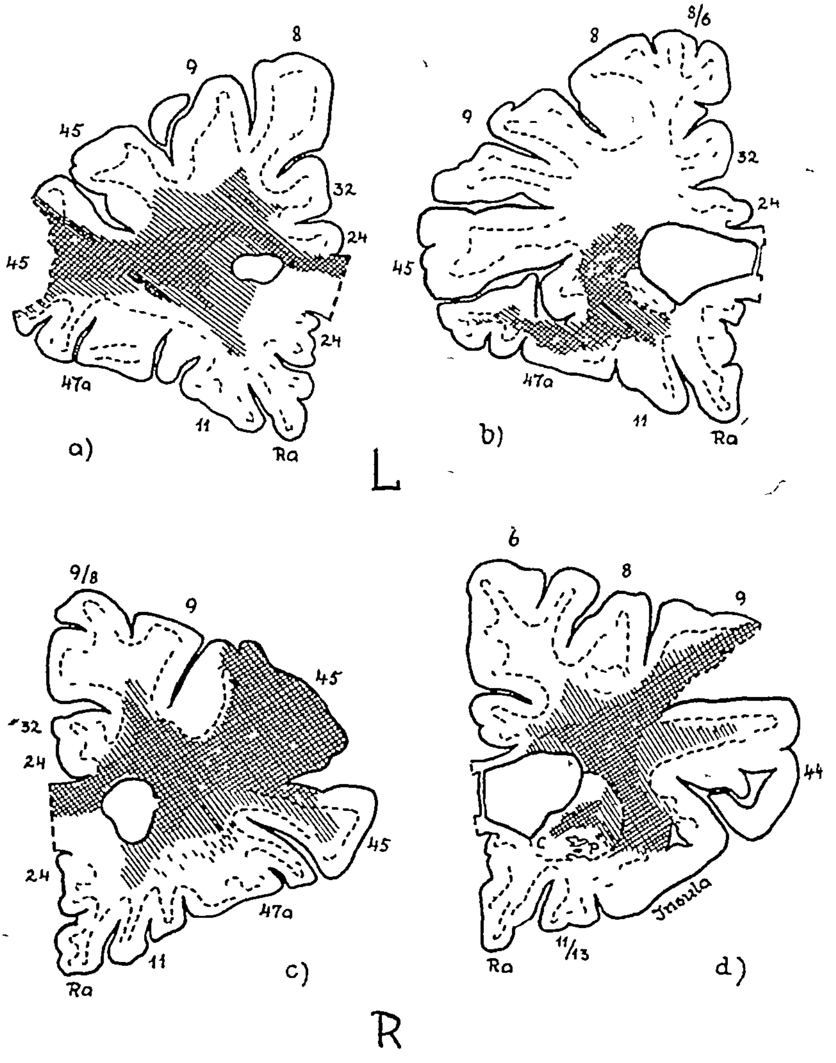

Fig 2—Greatest extent of surgical lesion in frontal lobes (hatched areas) Numerals indicate Brodmann s cyto-architectonic fields in each section C, caudate nucleus ; P putamen Ra, area recta anterior

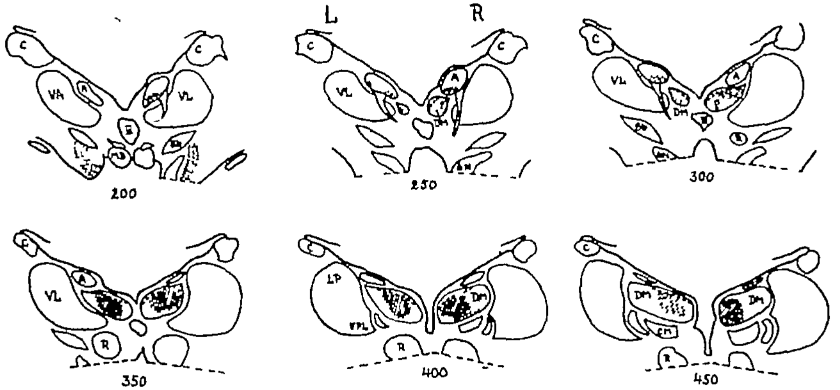

Fig. 3—Retrograde degeneration in thalamus (hatched areas): A, nucleus anterior thalami; C, nucleus caudatus; DM, nucleus medialis dorsalis thalami; LP, nucleus lateralis posterior thalami; MB, corpus mammillare; R, nucleus ruber; Sb, corpus subthalamicum; SN, substantia nigra; VA, nucleus ventralis anterior thalami; VL, nucleus ventralis lateralis thalami; VPL, nucleus ventralis posterolateralis thalami; III, ventriculus tertius.

graphically in fig. 1. In the second test, 29 days after the operation, the fall in both systolic and diastolic pressures was much less than preoperatively, the initial readings being much lower and the lowest reading very slightly higher. The *resistance of the palmar skin* was measured on several occasions before and after the operation. This technique has been described elsewhere together with the results obtained with patients undergoing prefrontal leucotomy (Elithorn et al. 1954). Recordings were made from both hands. No consistent difference between the two hands was observed, and in fig. 1 the mean values for the two hands are given. It is apparent that all except one of the immediately postoperative values are higher than those found before the operation. The postoperative reduction in palmar sweating which generally follows prefrontal leucotomy has been shown to be independent of thermoregulatory requirements. It is probably related to the relief of anxiety which normally follows the operation. After the operation there was a considerable change in *weight*. In February, 1949, the patient weighed 9 st. $7^1/_2$ lb.; 2 years later she weighed 13 st. 5 lb. Strenuous attempts were made to keep her to a diet, and her weight fell to 11 st. 10 lb. On her last visit, in November, 1952, she weighed 11 st. $4^3/_4$ lb. Throughout the follow-up period she continued to complain of *insomnia*, which, however, was adequately controlled with hypnotics.

*Pathology*.—The brain weighed 1430 g. and showed considerable atheroma of all the arteries at the base, especially the vertebral, basilar, and carotid arteries. There was a slight bilateral tonsillar pressure cone. Both frontal lobes, particularly on their anterior and dorsal aspects, were somewhat atrophic. The leucotomy entry marks were in the pars triangularis of the inferior frontal convolution on either side. A coronal section through these entry marks at the level of the genu corporis callosi passed through the greatest extent of the leucotomy scar (fig. 2*a* and *c*). This occupied almost the entire white matter of both frontal lobes, extending to the wall of the lateral ventricle, which was pierced on the right side; the two scars communicated through the dorsal half of the corpus callosum. Only the most medial dorsal and orbital regions had escaped. The cortex of both inferior frontal convolutions was extensively damaged. More posteriorly, at the level of the head of the caudate nucleus, the lesion in the left hemisphere (fig. 2*b*) was much smaller and terminated in a central and ventral position, slightly involving the caudate nucleus. The lesion in the right hemisphere at this level (fig. 2*d*) was still extensive and occupied, in addition to those structures mentioned above, parts of the striatum, the claustrum, and the capsulæ externa and extrema. It terminated 5 mm. further posteriorly in a similar position. Anteriorly the lesions extended within the central white matter to the level of the pregenual gyrus cinguli on either side. Histological investigation of serial sections through the thalamus (fig. 3) showed substantial retrograde degeneration in both dorsomedial nuclei (the right more than the left), moderate degeneration in the right anterior nucleus, and slight changes in the left anterior nucleus. There was considerable nerve-cell loss, shrinkage, and a dense compensatory gliosis. From the site of the degeneration within the thalamic nuclei and from the histological investigation of the surgical lesions one can conclude that the thalamic connections with Brodmann's areas 8, 9, 10, 46, 45, 47, lateral 11, and 24 were severed. All these areas were more severely involved on the right side than on the left. Further, a few fibres to the left medial orbital gyrus rectus were interrupted. In addition to the thalamofrontal projection, the fasciculus cinguli, the superior longitudinal and uncinate fasciculi, and Arnold's bundle were cut bilaterally. Representative blocks from various cortical regions showed no gross damage but some increase of the marginal glia and of the fibrous glia in the white matter. Most blood-vessels, both of the brain and the meninges, showed adventitial fibrosis; the larger and medium-sized arteries showed various degrees of arteriosclerosis.

## Discussion

In view of the current preference for selective "bimedial" incisions this case is of considerable interest. It is clear that the operation aborted a severe hypochondriasis occurring at the involutional age. Pathological investigation has shown that this result was achieved in the absence of significant damage to, or involvement of, the medial orbital regions, and with only unilateral involvement of the cingulate areas. In the light of these findings it seems worth while to examine the evidence on which the current preference for bimedial operations is based. In doing so it becomes necessary to consider whether an operation which produces statistically "maximal improvement with minimal personality change" is necessarily the operation of choice in any given patient.

Much of the enthusiasm for the bimedial operation stems from the results of the Massachusetts lobotomy studies (Greenblatt and Solomon 1952). These workers have in fact only shown that in *schizophrenics* this operation produces results which are more satisfactory than either a standard bilateral operation or a unilateral one. They do not themselves provide any evidence on which the different symmetrical modified cuts can be compared. Their original preference for this operation is perhaps based on the earlier work of Scoville et al. (1951), who reported the results obtained in an [illegible] tigation which compared the effects of three [illegible] undercuts, superior medial cingul [illegible]

These workers, the majority of whose patients were also *schizophrenic*, concluded that there was little to choose between the three areas from the point of view of therapeutic effect, but claimed that there were definite differences between the postoperative syndromes characteristic of each area The superior-convexity operation, they stated, was associated with the most striking personality changes, in particular emotional blunting and apathy After an orbital cut the personality showed less change, this being in the direction of hyperactivity and restlessness Medial cingulate operations they reported as causing postoperatively a severe physical "knock out," again with little personality change These results contrast strongly with those of Le Beau (1952), whose patients also underwent various forms of topectomy and undercutting Le Beau agrees that operations on the convexity tend to produce the greatest personality change, in his cases, however, this was in the direction of overactivity—"the hypomanic syndrome of the convexity"—whereas orbital cuts produced apathy

Similar inconclusive findings have also been reported after clinicopathological investigations Thus, reviewing the results obtained from their study at the Institute of Psychiatry, Meyer and Beck (1954) conclude

> "The dorsal and, in particular, the dorso lateral sectors of white matter do not appear to be as significant for improvement as the midcentral, orbital and cingulate sectors On the other hand, involvement of the dorso lateral and lateral white matter, and particularly cortex, appears to be one of the factors responsible for severe personality change" However, they point out that "full social recovery was obtained provided the cut was quantitatively adequate without consistent involvement of medial, orbital, and cingular segments"

Eie (1954) reports the macroscopic necropsy findings in 29 cases and claims that his results show that

> "aggressive, hyperactive, restless patients may improve after lesions limited to the connections of the granular areas of the convexity and of the cingulate gyrus"

One important difference between various workers is that the selection of patients differs widely from one investigation to another Both pathological investigations were undertaken largely on patients who died in mental hospitals The Maudsley material was diagnostically mixed, whereas those of Eie's patients who were suitable for clinicopathological analysis were all overactive and aggressive before operation In the two clinical series discussed the contrast is even greater most of Scoville's patients were *schizophrenics*, whereas most of Le Beau's were operated on for *intractable pain*

The striking contradictions between the results found by these and other workers suggest that ablations of anatomically corresponding areas need not produce similar defects in different patients Indeed, most clinicians will agree that their expectations of the sort of defects which may follow any individual leucotomy are coloured by the previous personality of the patient

The conception that there exists an operation which will produce the greatest improvement together with the smallest personality change is based on the belief that improvement and personality change are two independent variables On theoretical grounds, and these are supported by clinical observations—in particular Partridge's (1949) important observations on depressive illnesses treated by leucotomy—it may be presumed that two major effects may be expected from frontal ablations

(1) Such a lesion may abort a functional psychosis (e g , an endogenous depressive illness) which in other circumstances might be expected to resolve spontaneously or to be resolved by treatment (e g , electric shock) For this effect the surgeon would seek to damage the area which would produce the greatest "shock" effect together with the smallest persisting disturbance of personality and intellect

(2) The main effect of a prefrontal ablation is to produce of personality which is generally characterised by a reduction in anticipatory and preoccupative activity Such a change, if not too extensive, may sometimes be in all ways beneficial, and is then sought deliberately in the surgical treatment of psychoneurotic disturbances of personality In other cases it might be necessary to produce these changes to an excessive degree so that a diminished personality should react with less emotional disturbance to an otherwise intolerable *strain*—e g , excessive *pain*, and the experiences of a schizophrenic psychosis (Frankl and Mayer Gross 1947) The surgeon seeking to obtain solely an alteration in personality structure would wish to cause the least structural damage compatible with achieving the desired effect—i e , he would choose to operate on the region known to be most likely to produce the type of personality alteration which was desired

Applying this type of analysis to the present clinicopathological case report one may argue that the successful results were closely associated with, and dependent on, the alterations in personality which followed the operation There was in the history and on examination little evidence that the illness might be an endogenous depressive one Although the onset was during the involutional period and followed a minor physical illness, there was no diurnal variation of symptoms, no retardation, and no objective sign of depression The clinical picture was essentially one of preoccupation with, and elaboration of, a disturbance of sensation It can be explained most economically as a reactive development of the patient's premorbid personality tendency to anxious preoccupation of the obsessional type This excessive reaction may perhaps have been partly precipitated by arteriolar and psychological stresses associated with the involutional period The changes in personality which followed leucotomy, and which justifiably came to be characterised as defects—i e , her laziness, her placidity and her lack of concern for herself, her property, and her relations—can be seen as a reduction in her tendency to ruminative and anxious preoccupation. Two main qualitative differences between her bothering less about her symptoms and her bothering less about her cooking and her finances seem to be (1) that the stimulus of the tinnitus was always present, and (2) that taking thought about the noises would not reduce their intensity Failure to habituate to a constant and irreducible source of emotional distress is characteristic of the neurotic personality and especially of the obsessional neurotic It is therefore likely that the change of personality involving a reduction in preoccupative anxiety was essential to the success of this operation, and that this personality change was undesirable only in so far as it was excessive

As regards the involvement of the orbital and cingulate regions, it appears that, since the operation was both successful and excessive, a further extension of the lesion would only have increased the defects To have cut the orbital and cingulate sections in place of an equal amount of dorsal tissue would (according to most workers) have produced less personality change But (most authorities would again agree) a similar effect would have been produced more economically by reducing the amount of dorsal tissue cut Later experience with modified leucotomies in non psychotic patients crippled by a morbid preoccupation with a tinnitus has in fact shown that operations restricted to the convexity, as well as bimedial cuts can produce relief with only minor personality changes These changes may in their own right be regarded by close relations as beneficial (Elithorn 1953)

We may conclude that the search for an operation which is statistically most satisfactory for all patients is sterile Both the relevant published reports and the analysis of the present clinicopathological report support Fulton's (1951) contention that restricted leucotomies should be adapted "to the nature of the mental illness" Fulton suggests that depressed patients should have the bimedial type of operation, and that those who are overactive or agitated might benefit most from a dorsal topectomy It is only necessary to point out that a causal clinical analysis is more important and relevant than an *observational correlation* which will depend on the sample of patients examined Many patients are agitated and overactive because they have a "depressive" illness

## Summary

The clinical history of a patient incapacitated by preoccupation with severe tinnitus and who was treated successfully by a 'standard' prefrontal leucotomy is reported together with a description of the primary lesions and the retrograde degeneration in the thalamic nuclei

The concept that there is a single selective operation which will provide in each case the greatest improvement with the smallest personality change is dismissed as unlikely

The relative rôles of 'improvement' and "personality change" in producing a satisfactory therapeutic result are discussed

We are particularly indebted to Dr Eliot Slater and Mr Harvey Jackson under whose care this patient was, and we would also like to thank Dr E A. Carmichael and Prof A Meyer for encouragement and advice Miss M. A Crosskey assisted with the autonomic investigations We are also indebted to Dr W A Cobb and Prof O L. Zangwill in whose departments the electro-encephalographic and psychological studies were made

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# Preliminary Communication

## BLOOD CONCENTRATIONS OF PYRUVIC AND α-KETOGLUTARIC ACIDS IN NORMAL PEOPLE AND DIABETIC PATIENTS

THE blood levels of α keto acids in patients with diabetes mellitus have attracted interest in recent years with the development of more specific and accurate methods for determining these important metabolites Villano[1] claimed that the blood concentrations of pyruvic and α ketoglutaric acids were greatly increased in diabetes but other workers[2 3] have reported raised blood levels of the two acids in only about half their patients, and Von Marken and Florijn[4] stated that the blood pyruvate level was normal in diabetic coma Conflicting results have also been obtained with animals Fidanza and Laviano[5] reported increased blood α ketoglutarate levels in alloxan diabetic rats whereas Frohman et al[6] observed that the tissues of alloxan-diabetic rats possessed a normal content of pyruvic acid but decreased levels of α ketoglutaric acid

The methods used have usually been based on the formation and subsequent separation by paper-chromatography of the 2 : 4 dinitrophenylhydrazone derivatives of the α keto acids. However 2 4 dinitrophenyl hydrazine is not a completely satisfactory reagent for this purpose because it is not specific for the α keto acid grouping and also because the derivatives tend to give rise to multiple spots during paper-chromatography from separation of geometrical isomerides[7] The first objection is of particular relevance when specimens from diabetic patients with ketosis are examined, because interference from aceto-acetic acid may occur when high concentrations of this substance are present[8]

BLOOD CONCENTRATIONS OF PYRUVATE, α KETOGLUTARATE AND GLUCOSE IN NORMAL AND DIABETIC SUBJECTS (MG PER 100 ML.)

| — | | Pyruvate | α-keto glutarate | Glucose |
|---|---|---|---|---|
| Diabetic patients (8) | 1 | 0·35 | 0·14 | 200 |
| | 2 | 0·33 | 0·06 | 91 |
| | 3 | 0·50 | 0·10 | 208 |
| | 4 | 0·31 | 0·05 | 250 |
| | 5 | 0·13 | 0·10 | 124 |
| | 6 | 0·20 | 0·08 | 350 |
| | 7 | 0·44 | 0·07 | 190 |
| | 8 | 0·86 | 0·14 | 72 |
| Mean ± standard error | | 0·44 ± 0·19 | 0·09 ± 0·03 | 211 ± 93 |
| Normal subjects (7) | Mean ± standard error | 0·35 ± 0·07 | 0·10 ± 0·02 | 96 ± 10 |
| | Range | 0·27 – 0·47 | 0·08 – 0·13 | 67 – 113 |

We have devised a method for the separation and estimation of pyruvic and α ketoglutaric acids in blood using 1 2 diamino-4 nitrobenzene which was introduced by Hockenhull and Floodgate[9] as a specific reagent for α keto acids with which it forms stable derivatives separable by paper chromatography The reagent is allowed to react with the deproteinised blood filtrate for 12–16 hours, and the derivatives are extracted with ethyl acetate and removed from the organic solvent with 5% *w/v* sodium carbonate solution After acidification of the sodium carbonate solution the derivatives are re-extracted with ethyl acetate, which is then evaporated to dryness the residue is dissolved in acetone and the derivatives are separated by paper-chromatography[10] The separated derivatives are eluted with 30% ethanol and the optical densities of the resulting solutions measured at 280 mμ

The blood pyruvate α ketoglutarate and glucose concentrations in 7 normal people and 8 ambulant diabetic outpatients are given in the table. All the patients were receiving insulin and were healthy apart from their diabetes 2 had a moderate degree of ketosis Rothera's test of their urine being moderately strongly positive at the time the blood samples were taken Inpatients or patients with intercurrent illness were excluded from the diabetic group to make it as comparable as possible with the group of normal people

The results show that there was no significant difference between the two groups in the blood levels of α keto acids. In the diabetic patients there was no correlation between the blood concentrations of glucose and of the two α keto acids

It appears therefore that in this series of patients the diabetes was not associated with any disturbance of the blood levels of pyruvic or α ketoglutaric acids over a wide range of blood glucose concentrations We propose to extend our studies to include analysis of the urine and also to investigate the blood concentrations and urinary excretion of pyruvic and α ketoglutaric acids in hospital patients with more severe diabetes

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# Medical Societies

## ROYAL SOCIETY OF MEDICINE

### A Children's Psychiatric Unit in a Mental Hospital

AT a meeting of the section of psychiatry on Dec 14 with Dr W MAYER GROSS, the president, in the chair, Dr J B ROGERS described an inpatient children's psychiatric unit which has been in action at the Crichton Royal Hospital for $3^1/_2$ years

The unit (which is not the first of its kind) is, he said, contained in three houses outside the hospital grounds, each capable of taking twenty children At Ladyfield, the first house to be acquired, there are twelve boys and eight girls aged 5–14, all of normal or better intelligence Organic disorders, behaviour difficulties, psychoses, and maladjustment are represented among them They normally do ordinary school work throughout their stay, under the care of one full time and one part time teacher Some, however, when they first come, do no school work for a few days, or only 2 hours daily for a time, depending on their mental and emotional state At times a special course (called something like "domestic science") is devised for a much disturbed child, which means in effect that he has a nurse to himself for a few days The school week is varied by swimming on two afternoons in the hospital swimming-pool (and the children never enter the main hospital grounds at other times), a Wednesday visit to town to spend pocket-money, church on Sunday, and a picnic trip to country or seaside on Saturday All activities are voluntary, but Dr Rogers finds that the children are more secure if they have a regular routine even the rebellious like a framework to rebel against True discipline is based on the bargain the child makes with life "I will give up this gratification to retain your approval" To help him towards making this bargain the nurses must be secure in themselves , and they must be able to give affection steadily all the time They also need to know what stage the child has reached , and in the weekly discussions with the psychotherapist all the nurses attend and are encouraged to talk about what they have noticed The educational psychologist, the teachers, the occupational therapist, and the psychiatric social worker also attend Those who spend most time with the children are junior nurses, or cadets and they often make valuable contributions Ladyfield is staffed by three senior nurses (one a man), three assistant nurses, and five cadets , and all the domestic work is done by the nurses Ward-maids are apt to become the recipients of confidences and to form relationships with the children which are outside the therapeutic scheme, so it is necessary to do without them Dr Rogers gave examples of three groups of children and their treatment—those with educational difficulties, those who had been unable to cope with stresses in their surroundings, and psychotic children

One child, aged 9, had been at school for 4 years and was unable to read or write Tests showed him to be above average in intelligence but suffering from word blindness This had caused emotional disturbance with panic reactions After two terms of special teaching and individual help he was able to go to a special school, and later to an ordinary school Another boy of good intelligence, who had become stone deaf after treatment for tuberculous meningitis at the age of 7, expressed his frustration in severe temper tantrums He settled well, and was able in time to go to a deaf school

A girl of 8 the middle daughter of three, was rejected by both her parents and responded to stress by enuresis and encopresis She wandered about apart from the other children, but accepted the chance of daily interviews with Dr Rogers and finally spoke out her fear that she would never have a happy life because nobody wanted her The sister in charge of the unit then began to give her special attention and establis[illegible] rm relationship Thus encouraged, the child [illegible] little trouble in the dormitory banding first with two younger girls to tease an older one, and later with the older girl to tease one of the youngsters Each of the teased children had to be fortified by the affectionate attention of a nurse of her own The patient next made trouble in the occupational therapy class, and this too simmered down in time Such "testing out" behaviour on the part of an insecure child is common, and this child was also enjoying the experience of having her two sisters—vicariously—under her thumb She improved steadily all round

Psychotic children present a very difficult problem, but Dr Rogers finds that individual therapy can produce, if not recovery, at least a remission

One psychotic boy of 7 wandered alone and used infantile speech , yet he could tell the time at a glance and knew his tables up to 24 times He was given individual therapy by a woman doctor with whom he would spend at first only 10 minutes at a time Later he would stay for $^3/_4$ hour, and took *to climbing on her knee and showing infantile curiosity in her* breasts A visit from his parents caused him to withdraw again, and they were advised (contrary to all usual custom) not to visit for 3 months At the end of that time he had improved and made relations with other children He went home for 6 weeks' holiday and got on well, though his mother was not fully able to tolerate his infantile sexual curiosity On his return he played better with other children, and a second holiday at home was more successful He now appears to be almost a normal boy During his treatment the nurse had to be reminded not to leave him alone to play by himself it was only individual attention that kept him in touch with his surroundings

The psychiatric social worker sees the parents when they visit—usually on Saturday and Sunday—and the parents and home are brought into the therapeutic scheme from the beginning Some of the children come from institutions, and the unit makes the same approach to those responsible for them as it does to the parents

At Ladyfield West, the second house, the children are quieter than those at Ladyfield no hyperactive children are taken, and the atmosphere is more tranquil The third house, Hannahfield Hall, receives children with both mental and physical handicaps—for instance, a mentally defective and blind spastic girl, and a boy withdrawn in catatonia The psychotic boy already mentioned is in Hannahfield Hall, but now he only sleeps there, spending all his days at Ladyfield

The objects of the unit are to provide an environment in which the child gets the benefits of a good home influence (the mother and father figures being provided by the nursing staff), regular schooling, and hospital treatment In the interests of research each child has an ordinary case history folder, and also a separate research folder in which all that is known about him is summarised weekly Behaviour is also recorded on a chart, and these charts are already throwing light on the natural history of psychiatric disorders in children It is a common experience that the beginning of improvement does not necessarily mean improved behaviour

In a child of 11 encopresis was replaced, after 4 weeks' treatment, by violent aggression The mother, not too pleased said she had preferred him as he was *It turned out that her husband (whom she had always described as "ineffectual") had at times been imprisoned for assaulting her*

Dr Rogers hopes to follow up as many of his cases as possible for 20 years He is also trying to see all the maladjusted children in a rural area, and hopes to compare their development with that of normal children in the same area

In deciding whether or not it is important that such a unit should be part of a mental hospital he gives great weight to the part played by the nurses They must be secure maternal people, able to give love and devotion but in no sense "deprived parents" Teachers have a different function, and so have occupational therapists their part in the therapeutic scheme is primarily to teach The approach of a teacher necessarily didactic to some extent that of a nurse maternal Nurses from the hospital can be tried out in the unit and given plenty of attention while they are new to the unit Those who are interested and have a flair for the work want to stay He emphasised too the value of cadets These young girls, aged 16 and 17 are hand picked from local families and because they are young enough to enjoy playing games with the children they are a great asset, and do a first-class job He also believes that child psychiatry should not be divorced from adult psychiatry they are parts of a whole picture

### DISCUSSION

Dr D E **Sands** described the male and female juvenile departments in the grounds of St Ebba s Hospital These take boys and girls aged 12–17 He finds that sometimes a few young women from the adult wards can be suitably transferred to the female juvenile ward to the advantage of the girls Conversely boys of 16–17 sometimes do better in an adult ward The neurotics and psychotics among these young people mix well but they are intolerant of the psychopaths among them The more disruptive psychopathic girls, he finds, often settle better in a ward of young adults suffering from chronic psychoses here their antisocial activities receive neither stimulation nor response from their fellow patients in fact they get a chance to shine by contrast, and become quite helpful The difficulty is to know where to send them after treatment they usually have to go into care elsewhere, whereas most of the neurotic and psychotic patients are able to return home A special hospital for adult psychopaths has been projected but it would be incomplete without a similar one elsewhere for juveniles The phases in development in mental illness in the young are not clear cut but a not uncommon sequence in boys is from an anxiety provoking situation to a behaviour disorder then via an obsessional stage to schizophrenia and in girls anxiety is more often converted to hysterical neurosis and then to schizophrenia The transition from one phase to another can happen within a week This suggests he said that there can be no real separation of neurosis from psychosis and that these terms merely indicate stages in the development of mental illness Finally he regarded the establishment of units for children or for juveniles as within the normal scope of a mental hospital and a further stage in the fulfilment of the needs of the community by these hospitals

Dr **Kenneth Cameron** spoke of the variety of demands made on a unit such as that at the Crichton Royal It must provide an observation and diagnostic service intensive group and individual treatment and care for long term cases The first service is often hampered by the fact that once the diagnosis is made it is necessary to provide treatment and places are scarce If the child needs to be transferred to a suitable educational centre it is not always within the power of the unit to arrange the transfer He agreed heartily with Dr Rogers about the importance and value of the nursing care well trained psychiatric nurses he said adapt themselves well to the needs of child patients

In the ensuing discussion it was urged that schools for the maladjusted should not be used as an alternative to treatment in a unit such as that described The presence of psychotic and psychopathic children in such schools can greatly hinder the treatment of the children who should properly be there Dr **Rogers** agreed that maladjusted schools ought not to be used in this way He does not however care to apply the term psycho path to any child It is generally used of children who have been kicked around for years and are unable to form a relationship with anybody Given individual treatment they do at last respond and form relations with other people—at least he has not yet met one who failed to do so But it takes at least 5 years and perhaps there are exceptions he will know better in 20 years time It was also suggested that this kind of unit might well be attached to a children s hospital to which the psychiatrist might come. Good pædiatric nurses speakers pointed out can also adapt themselves to children with psychiatric problems Dr Rogers agreed on the importance of a close link between pædiatricians and psychiatrists doing this work but reminded the meeting that the equipment of a mental hospital is of service an electro-encephalograph for instance is there on the spot

Interrogated about adolescent problems destructive behaviour dancing pets and music he replied that as the children were young he had no adolescent problems He had no destructive behaviour either—or very little A greenhouse adjacent to the unit, used mainly to grow flowers for the delectation of the board of management had lost only 7 panes in $3^1/_2$ years and the children were much more destructive to the staff (in the sense of having rows with them) than to the place. A row he thinks is more satisfactory as therapy for aggression than the breaking up of coal or indeed of anything else for if the therapist goes on behaving like a reasonable person and liking the angry child the child gains security and the rows gradually stop Before the staff learned this the children took out the fireplaces and so on , but now that the staff know how to cope there is little destruction of property He encourages as many pets as the nurses will tolerate, but he finds cats get on best they have nine lives and need every one of them Country dancing singing games, and a percussion band provide the music as well as a local dance band leader with a piano accordion

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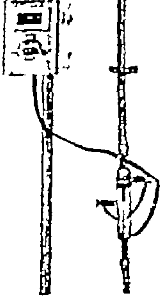
# New Inventions

## AN ELECTRICAL DRIP RECORDER

This apparatus, made for us by Messrs Matburn Ltd consists of a drip-chamber into which are fused two electrical wires so placed that the passage of a drop of fluid makes contact with them simultaneously This completes an electrical circuit which causes a small neon bulb to glow momentarily as each drop of fluid falls from the nozzle in the chamber A small dry battery provides the power for the light which is so arranged that there is no possibility of the patient s receiving an electric shock or of a spark The whole apparatus can be earthed.



In a ward at night this apparatus will enable a nurse to be sure that a drip is behaving properly and she will therefore have no need to use a torch which might awaken a sleeping patient. In the theatre the placing of the neon light on the anæsthetist s table remote from the drip will enable him to keep a check even when the table is surrounded by onlookers

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# Reviews of Books

## The Spino-cerebellar Degenerations

J G GREENFIELD, M D, F R C P, honorary consulting pathologist, National Hospital for Diseases of the Nervous System London Oxford Blackwell Scientific Publications 1954 Pp 112 17*s* 6*d*

CLINICAL neurologists have for many years moved ataxically through the eponymous wasteland of the spino-cerebellar disorders But Dr Greenfield's unrivalled experience of the clinical and pathological features of these diseases, added to his extensive knowledge of the literature, has given us an informative and authoritative monograph The wise man is rarely dogmatic where information is vague and uncertain, and he recognises that no differential diagnosis is possible during life between many of the different forms of cerebellar and spino-cerebellar disease

The scaffolding to the study is built from the historical and the pathological backgrounds to the spino cerebellar disorders A short (perhaps too short) account of the anatomical and physiological considerations leads to a comprehensive classification of the degenerations, which are ranged into three main groups—predominantly spinal, spino cerebellar, and predominantly cerebellar This classification is clear and concise, and takes into account the eponyms with which the subject is burdened Instead of adhering closely to his original outline Dr Greenfield selects only a few of the types for historical and pathological discussion, and he does so in such a way that at first order appears to dissolve once more into disorder But as soon as the reader realises that this elaborative section is intended as a commentary rather than a fully organised and comprehensive statement, he can settle down to a clear and detailed exposition of the historical, clinical, and pathological features of the many forms of these degenerations, with which so many neurologists and neuropathologists have perpetuated their own names, often at the cost of confusing the minds of their successors In this survey Friedrich receives due homage, Menzel, Holmes, Déjerine, André Thomas, and others are appreciated, but Marie is consigned to whatever eternity is reserved for the uncritical The monograph ends with some comments on blindness and dementia in association with the hereditary ataxias, and there is a full bibliography

Neurologists, neurosurgeons, and neuropathologists alike, will be grateful to Dr Greenfield for removing so many of the misapprehensions caused by unselective clinical and pathological work in the past

## Tumours of Lymphoid Tissue

GEORGE LUMB, M D, reader in pathology, Westminster Medical School Edinburgh and London E & S Livingstone 1954 Pp 204 37*s* 6*d*

IN this monograph, based on 410 cases of tumour of lymphoid tissue, Dr Lumb succeeds in dispelling confusion in one of the more difficult chapters in human pathology His style is lucid, the well-chosen photographs are excellent, and the statistical tables are useful

Hodgkin's disease accounts for 46 1% of the series, as against 19 2% for lymphosarcoma and 16 9% for anaplastic sarcoma The five year survival rate for Hodgkin's disease is 34 96% (the average survival is four and a half years) as against 62 3% for follicular lymphoma and only 5 26% for anaplastic sarcoma The five year survival rate for lymphosarcoma is 22 22% over the age of thirty five but only 12 5% below that age Dr Lumb objects to the common misuse of the term "reticulosis", to him it connotes a reaction on the part of pluripotential mesenchymal cells to varying stimuli, and as such the term is analogous to fibrosis and gliosis, therefore its use in a particular sense to denote a specific disease ("one of the reticuloses"!) cannot, he says, be justified Certainly nomenclature and oncological classification can be simplified if one accepts his contention that the variation in structure of the tumours and degree of malignancy is due to the cell type *differentiation* from pluripotential cells

The book will be invaluable to the many who are concerned in the giving of prognosis As in other tumours, anaplasi [illegible] of malignancy, but there are occasional [illegible] the prognosis proves to be better than the histological appearance had suggested There are good sections on biopsy technique, including the recognition of *artefacts*, the effects of radiation, and problems in differential diagnosis There is also a bibliography and an interesting historical survey

## Leukæmia Research

*A Ciba Foundation Symposium* Editors G E W WOLSTENHOLME, O B E, M A, M B, MARGARET P CAMERON, M A, A H-L S, assisted by JOAN ETHERINGTON London J & A. Churchill. 1954 Pp. 297 30*s*

THE selection of leukæmia research for this symposium is due to the European scientific advisory committee of the Lady Tata Trust, and many of the workers invited have been supported by the trust at some time The result is a comprehensive account of current research in which all points of view are represented

Here will be found accounts of the multiplying chemotherapy, and what still remains for radiotherapy, there is a notable discussion on the virus transmission of mouse leukæmia, and at several points the question of how far these animal studies are applicable to the human disease is discussed. Fowl leukæmia studies are now less important and there is little on cell morphology Furth presented his concept of *conditioned and autonomous neoplasms*, an idea that may well be fruitful in leukæmia The account of the effect of ionising radiations has a topical interest.

This volume forms a most useful starting-point for anyone contemplating research in this field, and is a valuable summary of growing-points for those actively working in hæmatology

## The Billroth I Gastric Resection

*With particular reference to the surgery of peptic ulcer* HORACE G MOORE, JUN, M D, formerly instructor in surgery, University of Washington School of Medicine, HENRY N HARKINS, M D, PH D, F A C.S, professor of surgery, University of Washington School of Medicine Boston Little, Brown & Co London H K Lewis 1954 Pp 176 52*s* 6*d*

THIS short and beautifully produced book is a plea for the Billroth-I gastrectomy, particularly in the treatment of duodenal ulcer Chapters 5 and 8 contain the main meat in the volume The former gives the technical details for performing the operation, and the excellent drawings of the Von Haberer-Finney end-to-side anastomosis of the stomach to the duodenum are convincing evidence that the scars of duodenal ulceration are no bar to a safe gastroduodenal junction Chapter 8 weighs the evidence for and against the operation and reaches a favourable verdict There is much else to interest gastric surgeons, including some historical notes on gastrectomy in general, and a review of the literature on the dumping syndrome, in which British work receives full attention Gastric surgeons, whether they can or cannot afford to be without this book, should certainly read it

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**Scientific Books, Libraries, and Collectors** (London The Library Association. 1954 Pp 288 24*s*)—Mr J L Thornton, the librarian of St Bartholomew's Hospital Medical College, has followed his learned history of *Medical Books*, published in 1949, with an even more ambitious volume, compiled with Mr R I J Tully of Bangor, on the history of scientific literature They bring into readable compass information which is not easily accessible, and offer a readable history of science from a new angle Instead of recording the great discoveries and advances in scientific knowledge, they plot the course taken by each scientist in making his work known In this way they guide the inquirer to the original sources for our knowledge of scientific discoveries The book covers all sciences, other than those strictly medical, from the ancient world to the end of the 19th century There are informative chapters on the growth of scientific periodical literature and of scientific societies The mathematical sciences are less fully covered than the biological, and any doctor would enjoy a great part of the book He might begin, for example, with pages 150 to 160 where the writings of the great 19th century biologists, both field naturalists and laboratory men, are admirably surveyed and implicitly related to the work of Charles Darwin

THE LANCET

*LONDON SATURDAY JAN 1, 1955*

## With which we Serve

A large nation cannot live on a small island, and enjoy modern amenities, unless its people are willing to accept much more regulation of their lives and work than our forefathers would have tolerated. What we in Britain are trying to achieve is a proper balance between the claims of the community and the claims of the individual, and we hope to prove ourselves politically capable of creating order without imposing uniformity—of reaching the next millennium without passing through *1984*. Seen in this larger context, the National Health Service is an attempt to devise a system in which medical work can be publicly financed and comprehensively planned, but in which the essential liberties of patient and doctor are preserved. After six and a half years experience an unprejudiced observer would probably say that, for all its defects, this vast and complex organisation has worked on the whole surprisingly well, and the Ministry of Health's recent review of five years progress[1] is in many ways encouraging. But initial progress does not necessarily imply ultimate success, and our ingenious compromise may yet justify the pessimists—either because in the long run, it does not promote efficiency, or because it does not maintain freedom, or even because it does neither.

How the experiment turns out will depend largely on what doctors think and do about it and, as a matter of fact, different people have quite different ideas about the fundamental nature of the N.H.S., according to which of its purposes they regard as primary. With its powers of regulation and planning uppermost in their mind, many doctors, and also many laymen, see it simply as an instrument of government: having assumed responsibility for all medical care the State discharges this responsibility through a chain of command reaching from the Minister in Whitehall to the practitioner in his surgery. On this view every hospital is a branch establishment of the Ministry and every doctor is a medical officer whose principal duty is to perform the tasks allotted to him keeping most carefully to the rules. This is of course the simple readily comprehensible pattern of a State medical service, which so often strikes the layman as just what is needed and it is the pattern which we may eventually get if we make the mistake of supposing that it is here already. In point of fact, elaborate precautions were taken to prevent the N.H.S. from being a crudely authoritarian service of this kind, but if doctors themselves neither notice nor care about the difference how should the laity know better? Every time that one of us—either out of irritation or in earnest—talks of a 'State doctor' or a "State patient" he brings nearer the day when doctors and patients may be just that. On the other hand, this day need never come if the profession fixes its mind, and sets its heart, on securing what was originally intended:

> 'Though the Minister of Health took wide powers which he could hold in reserve, the Government's avowed object was to integrate, support, and supplement the work of existing medical agencies rather than to unify, regulate or supersede them. The N.H.S. should in fact be regarded not as a centralised service, in which the hospitals and doctors at the periphery exist to carry out central instructions, but rather as a confederation of medical institutions whose activities need coördination and sometimes leadership. It is these institutions, varying in size from the single-handed practice to the large hospital, that actually look after patients; and, whether as individuals or groups, they develop their own *methods and standards.*"[2]

In this concept of a confederation of institutions with its emphasis on variety and initiative, we have the antithesis of, and the alternative to, the kind of State medical service which emphasises uniformity and control.

In the closing months of his life Sir JAMES SPENCE gave much thought to the contrast between services and institutions as means of providing medical care. Unfortunately, the fragment of his last lecture which we publish this week does not contain his definition of an organised service, but he might have agreed that such a service is an undertaking in which the requirements of an authority are fulfilled by the servants of that authority. Since Parliament has decreed that medical care shall be provided and has made a Minister responsible for seeing that this is done, it has been necessary to establish an administrative service in which the Minister's servants are under a duty to carry out his instructions. To this extent the N.H.S. is in fact a centralised service under the State. But it ceases to be a service at the point where administration ceases and medical work begins, for clinicians are in no sense servants of the Minister but only of their patients. In the end what really matters is not the service—the enabling device—but the actual institutions large and small through which patients are helped, and SPENCE was deeply anxious first that these medical institutions should be good, and secondly that every doctor should think of himself always as a member of the institution where he works and never as a member of some remote service. An institution he defined as the establishment and arrangement of human effort towards a common end, carried out by the covenant of one with another"—which is something different from carrying out orders. The institution may be a general practice or a cricket club or a hospital or even something so large as a university, but there is always a risk in excessive size; because in a large institution the sense of 'covenant' or of belonging to a group is common end, is all too apt to weaken or disappear In SPENCE's opinion the big hospital, with doctors who do not know each other, is liable to lose its status as an institution and become only a sort of service, whose personnel are merely performing duties instead of being concerned together in their chosen task

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[1] Report of the Ministry of Health for 1953. H.M. Stationery Office 1954 See *Lancet* 1954 ii 1169

[2] Memorandum of Evidence submitted [illegible] Physicians to the Guillebaud Co [illegible] 1 362

Does this philosophising lead anywhere ? Yes, if we recognise that, from the patient's standpoint, all that matters in the N H S is the excellence of its constituent institutions, and if we all—doctors and administrators alike—pay less attention to the service in the abstract and more to the means by which these institutions can be strengthened Is it not probable, for example, that the morale of some of our hospitals has been unnecessarily weakened by brigading them with others in a way that has removed their sense of identity ? In these days when we are preoccupied with establishing specialist " services "—orthopædic, obstetric, and so on—are the members of hospital staffs really given enough say in choosing their new colleagues ?[3] (Like marriages arranged by parents, appointments by outsiders are sometimes very successful, but they are by no means always the happiest start for thirty years' cooperation , and perhaps, as SPENCE believed, the post-war discouragement of institutional inbreeding has been carried to a point where it does more harm than good ) Finally, should not administrators give further thought to his remark that he knew of no example of a good hospital which has not been created through the good offices and good will of its medical staff ? The corollary to this is that damage is done when the medical staff either cannot or do not give guidance to the governing body Though the administrative decisions have to be made by the boards and committees which are part of the Minister's executive service, the doctor's responsibility and interest should be by no means confined to the care of his patient, but should extend throughout the institution of which he is a member

To organise the medical care of fifty million people on a high level, and at the same time ensure that professionally every doctor remains his own master, is an extraordinarily hard task , and we are all well aware that it may be made virtually impossible by such unfavourable factors as too little money, too much machinery, or even the rulings of judges who find no legal sanction for the doctrine of professional-responsibility—regarding the surgeon, like the boiler-man, as a servant of his board Even so, perhaps the most serious menace to the National Health Service comes from those doctors in it who feel that they have been conscripted into a service and therefore dissociate themselves from the effort to make it succeed In a small but important minority of cases this dissociation takes the active form of exploiting, or allowing their patients to exploit, an organisation towards which they feel no loyalty , but usually it manifests itself in nothing worse than a tendency to attribute all faults to " them " not to " us " When one recalls the original and deeply sincere opposition to the whole scheme, this latter degree of dissociation is indeed very far from surprising , but if (as we believe) the preservation of professional freedom in this country depends very largely on the success of the present experiment, it is a pity that any doctor should appear to want it to fail On the other side, however we must remember that, in medicine as elsewhere, continual criticism is a necessity , and also of course that the English are apt to speak disrespectfully of what they hold most dear—unless, indeed, someone else does so What any doctor says about the service does not, after all, matter nearly so much as what he does about the particular medical institution where he works Granted their present faults, it is these institutions that give us so much cause for both pride and confidence

## Anticoagulants for Myocardial Infarction

WE make no apology for returning to the topical subject of the management of the effects of coronary occlusion or insufficiency Since we last commented on this matter,[1] the Committee on Anticoagulants of the American Heart Association has published a study of 1031 cases The authors of this important account—IRVING S WRIGHT, CHARLES D MARPLE, and DOROTHY FAHS BECK[2]—justify its exhaustiveness by pointing out that every year about 200,000 persons in the U.S A die from myocardial infarction and 600,000–800,000 suffer attacks " Perhaps the greatest personal and social significance of myocardial infarction lies," they say, " in the large number of persons lost by death during their most productive years—years when their talents are most needed by their families, their professional or industrial groups and their nation " The figures of age-distribution emphasise this 16% of the patients in their series were aged 40–49, and 35 9% were aged 50–59 , and the patients were mostly males—87 3% of the first of these age-groups and 84 6% of the second The 1031 patients were divided into 589 who received anticoagulant treatment and 442 who did not and who served as controls Sixteen hospitals cooperated in the survey and used uniform methods of case taking and treatment The analysis of the symptoms shows that the well-recognised clinical picture is a correct one pain, fall in blood-pressure, pyrexia (100°F or more), increased erythrocyte sedimentation rate, increased pulse rate, and a white cell count of 9500 or more per c mm are the commonest findings, cardiac enlargement or failure and abnormal rhythms are less prominent

It is very clear that the danger of myocardial infarction, once the patient has survived the first twenty-four hours, lies in thrombo embolic complications , and it is also clear that the effectiveness of anticoagulant treatment lies in its ability to prevent these complications The American team conclude that anticoagulants substantially reduce all types of complication whether intracardiac or extracardiac including emboli originating in mural thrombi From the high rate of thrombo embolism in the first week of the illness and from the observed effects of delay in treatment, they recommend that anticoagulant treatment should be begun as soon as possible and the prothrombin level lowered as rapidly as possible The anticoagulant treatment should last for at least four weeks after the initial attack, and should thrombo embolism occur, the treatment should be continued for four weeks from the last such incident The team are in favour of long term anticoagulant treatment for patients with a record of repeated myocardial infarction. Protection is greatest when the prothrombin times are kept at between two and two and a half times the normal level (about 23% prothrombin or less) The association of anticoagulant therapy with reduction in the risk of thrombo-embolism though noted at all ages was greatest in the 50–60 age group but anticoagulants did not remove the upward trend of complications with increasing age The data suggested that without anticoagulant treatment the risk of thrombo embolism is greater in men than in women, but anticoagulant treatment reduces the incidence greatly in both sexes and rather more in men than women Consequently the team suggest that anticoagulant treatment is suitable for all patients regardless of age or sex The data support the view that anticoagulants are effective in both mild and severe cases both types will benefit from maximum protection from the onset The authors conclude that their results do not support the contention of RUSSEK and ZOHMAN[3] that 'good risk' cases—i e those with no unfavourable signs at their first examination—do not need anticoagulant treatment WRIGHT and his co workers are quite clear that good risk cases showed fewer thrombo-embolic complications when given anticoagulants, and they point out that the screening for good risk cases involves a great possibility of error

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[3] *Lancet* 1948 ii 101

[1] *Lancet* 1953 ii 171

[2] Myocardial Infarction Its Clinical Manifestations and Treatment with Anticoagulants By I S WRIGHT, C D MARPLE, and D F BECK New York Grune & Stratton. 1954 Pp 656 $8 50 See also *Lancet*, 1954, i 92

Provided that the prothrombin time is kept at two to two and a half times normal, the danger of hæmorrhagic complications is small lowering still further the prothrombin level increases the risk of hæmorrhage and gives no added protection against thrombo embolism To maintain a smooth level of prothrombin reliable laboratory control is essential and the committee are not in favour of giving anticoagulants without such control The hæmorrhagic complications during anticoagulant treatment have been exhaustively analysed Some evidence of bleeding was observed in 12 0% of the treated patients, but it was also found in 5 2% of the control group and in only 7 8% of the treated group was the bleeding ascribed to the anticoagulant No less than 54% of these bleeding episodes were mild (mostly microscopic hæmaturia), 30% were classified as moderate there were in fact only 4 severe bleeding episodes among the 577 treated patients considered and in only 1 was the anticoagulant clearly the sole factor causing the bleeding None of the clinically observed cases of hæmorrhage was fatal but some unsuspected hæmorrhages were discovered at necropsy in fatal cases. Nevertheless the team believe that the benefits of anticoagulant treatment greatly outweigh the risk of hæmorrhage Patients with complicating azotæmia or with renal diseases and to a lesser extent patients with liver enlargement or myocardial failure have a greater tendency to bleed but the added risk is not great enough for anticoagulants to be withheld

The data show clearly that administration of anticoagulants reduces the risk of death, during the period of observation only two thirds as many patients per 100 died in the treated group as in the control group (TUDHOPE and DONALD[4] have already described evidence suggesting that in survivors one month after myocardial infarction the mortality rate during the subsequent eleven months is considerably lower among those who have received anticoagulants than among those who have not) The reduction in deaths in the American series appears to be due primarily to the prevention of thrombo-embolic complications, since in 42% of the control group (compared with 23% of the treated group) death was preceded by clinically diagnosed thrombo embolic complications Furthermore the contrast in death rates between the control and the treated groups was greatest in the second, third, and fourth weeks when anticoagulant treatment was most effectively maintained The necropsy findings on patients who died showed that nearly three quarters of the original infarctions were due to thrombi and were "potentially preventable with anticoagulant treatment, provided the need could have been anticipated and therapy instituted in time" Coronary insufficiency accounted for 15% of the cases, and 11% were attributed to miscellaneous or unknown causes Only 3 4% of the original infarctions were due to subintimal hæmorrhages Calculations showed that rupture of the heart or intracardiac hæmorrhage was an immediate or contributing cause of death in 2 4% of the control patients and in 4 1% of patients who had received anticoagulants but in contrast the death rate from thrombo-embolic complication was reduced fivefold in the treated group All the same, the American team reasonably point out that the risk of intracardiac hæmorrhage should be reckoned with and watched for by clinicians treating patients with anticoagulants and that by good management of the anticoagulant control this risk can be minimised

It needs no great perspicacity to deduce from all this that the authors of the report are wholeheartedly in favour of anticoagulant treatment for *all* patients with myocardial infarction whether mild or severe They consider that treatment should be begun as soon as possible, using heparin if necessary for the first twenty four to forty-eight hours and be continued for four weeks 'provided no significant contra indications are present and the facilities are available for meticulous supervision of its administration.' These conclusions are the same as those reached by GILCHRIST and TULLOCH[5] from a study of 321 cases seen in Edinburgh over a seven year period The committee's report is concerned only with patients treated with dicoumarol or ethyl biscoumacetate but the use of newer anticoagulants[6] will not change their conclusions since these drugs make control more effective Opposing the conclusions of IRVING WRIGHT and his school RUSSEK and ZOHMAN[7] have reiterated their view that, by assessing eight important signs and symptoms it is possible to classify patients into good and poor risks and only the poor risk cases need anticoagulant treatment Of 1318 patients admitted to hospital with myocardial infarction 46% were classified on the day of admission as good risk cases and RUSSEK and ZOHMAN contend that for this large proportion of patients the mortality and incidence of thrombo embolism is so low that anticoagulant treatment, with its added risk of hæmorrhage, cannot be expected to improve the prognosis They also point out that most of the deaths in the good risk group occur in the first forty-eight hours, when anticoagulant treatment does not give protection, and thrombo-embolism after the first forty-eight hours is relatively infrequent So RUSSEK and ZOHMAN estimate that only 30% of all patients with myocardial infarction require anticoagulant therapy It is clear, from a series of questions and answers published by SCHNUR,[8] that American opinion is far from unanimous on this question The majority are taking a middle course HALPERN et al ,[9] for instance, administer anticoagulants in all cases for the first forty-eight hours, thereafter discontinuing this treatment where the prognosis is judged good. Others reach an immediate decision, withholding anticoagulants from patients with mild first attacks But the answers to SCHNUR's questions show that, since the public knows of these drugs, it is often difficult to withstand the relatives' demand for their use

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[3] Russek H I Zohman B I Lancet 1951 ii 910

[4] Tudhope G R., Donald A G. *Ibid* p 40

[5] Gilchrist A R. Tulloch J A *Brit med J* 1954 ii, 720

[6] *Lancet* 1954 ii 742.

[7] Russek H I., Zohman B L. *J Amer med Ass* 1954 156 1130

## Pulmonary Embolism

PULMONARY embolism, it is now realised, is much commoner than was formerly supposed In the aged and enfeebled its supervention may be stealthy and easily overlooked , indeed, it may deserve the title of the acute disease most likely to escape detection Sudden death from massive embolism after operation is familiar enough , and the case of the patient with obvious heart-disease or phlebothrombosis in the leg who begins to have pain in the chest, hæmoptysis, a pleural rub, and an abnormal shadow on the chest radiograph is rarely misdiagnosed But often the clinical picture of pulmonary embolism is far less typical Moreover, although good radiographs will nearly always reveal some abnormality,[10] radiographs of elderly obese invalids taken with a bedside apparatus are often not very helpful , and it is among such people that pulmonary infarction is most usual Necropsy figures such as those published by MORAN [11] and TOWBIN [12] leave no doubt about the frequency of this complication TOWBIN, for example, in 512 necropsies on the late inmates (mostly elderly folk) of a social-welfare institution at Columbus, Ohio, found emboli in the lungs of 25%, and of 34% where death had occurred after the age of 70 TOWBIN does not state exactly how many of these emboli had been diagnosed during life, but he makes it clear that many had been either overlooked altogether or mistaken for coronary thrombosis or bronchopneumonia TOWBIN has been at pains to compare the pattern of illness and death in his institution with that in the surrounding city , and he concludes that a similar incidence of pulmonary embolism is to be expected during terminal illness in older members of the general population Of course not every embolus discovered at necropsy has necessarily been the cause of death , in some the embolism may simply have been the coup-de grâce in a chronic illness Nevertheless a disorder that is so common , so dangerous is a serious challenge, which is likely to grow in importance as the population ages and other immediate causes of death, such as infection, are gradually eliminated.

The problem of pulmonary embolism is threefold how to prevent it, how to recognise it, and how to treat it In the absence of heart disease nearly all emboli come from clots in the deep veins of the legs [13] Not all the causes of such venous thrombosis are clear , but there is little doubt that in elderly people one important cause is enforced rest in bed, especially when this has been brought about by an infection, for some infections are known to be accompanied by an increased tendency to clotting of the blood Old folk tend to go to bed for comparatively slight illness, and in this they are often encouraged by well-meaning relatives They should, on the contrary, be prompted to remain ambulant as long as possible Postoperative phlebothrombosis is not easily prevented , early ambulation has not reduced its incidence LAMBERT ROGERS [14] believes that pressure by the operating-table on the calves of the legs can obliterate the intermuscular veins and predispose to clotting, and conceivably this may also be true of the frequently flinty hospital bed-mattress Pulmonary embolism from an unsuspected thrombus is particularly liable to occur when the patient first gets out of bed, and SHORT [15] has therefore suggested that anticoagulants should be given routinely during this danger period

The recognition of pulmonary infarction depends on constant vigilance Any older person confined to bed who suddenly begins to have unexplained pyrexia, dyspnœa, or chest pain should be suspected of having embolism and should be carefully examined for evidence of preceding phlebothrombosis Infarction is often particularly quiet when masked by existing heart-failure , but sometimes its onset is betrayed by unexpected tachycardia or cardiac arrhythmia [15] Once deep-vein thrombosis, with or without embolism, has been diagnosed, anticoagulants should be given unless there are strong contraindications With careful treatment the mortality risk is probably no greater than 2% or 3%, even among older patients The death-rate from pulmonary embolism after untreated femoral-vein thrombosis is of the order of 10% Unfortunately fatal pulmonary embolism is often unheralded [16] , but if embolism has already occurred, anticoagulants will reduce the likelihood of further embolism Intravenous trypsin has been used experimentally to dissolve intravascular thrombi, but it has not yet been proved to deserve a place in clinical practice[17] When there has been repeated embolism despite adequate anticoagulant treatment, it may sometimes be necessary to tie a vein , but ligation of large vessels, such as the inferior vena cava, is not to be lightly undertaken, for the late sequelæ are often disabling [18]

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[8] Schnur S *Ibid* p 1127

[9] Halpern M M Lemberg L Belle M Eichert H *Ann intern Med* 1954 41 942

[10] Short D S *Quart J Med* 1951 20 233

[11] M[illegible] *Amer J clin Path* 1947 17, 205

[12] [illegible] *J Amer med Ass* 1954 156 209

[13] Bauer G *Lancet* 1946 i 447

[14] Rogers L C *Congr Soc int Chir* New Orleans, 1949 p 511

[15] Short D S *Brit med J* 1952 i 790

[16] Marks J Truscott B M., Withycombe J F R *Lancet* 1954 ii, 787

[17] See *Ibid* p 904

[18] Shea, P C., Robertson R L *Surg Gynec Obstet* 1951, 93 153

# Annotations

## ACTION ON AGENE

THE Minister of Food's announcement, reported on p 53 of this issue, that manufacture of agenised bread is to cease at the end of 1955 is the tardy outcome of a disturbing discovery in 1946 In that year Mellanby[1] ound that agenised flour in large amounts induced "hysteria" in dogs; and it was shown to cause a similar disturbance in some animals other than dogs Rapid progress was made towards the identification of the toxic substance.[2] Meanwhile a committee set up to examine the suitability of this flour for human consumption reported in January, 1950 that though it had not been proved to be toxic to man its use should be discontinued[3] This recommendation the Government of the day accepted But in the intervening five years no action has been taken; and in answers to parliamentary questions the failure to act has been variously ascribed to the inevitable delay in conversion of flour mills to the need for finding a suitable alternative flour improver and to deferment of a decision pending the receipt of a report of an investigation under the ægis of the Medical Research Council This report to which the Minister of Food referred in his statement confirms that agene treated flour induces fits in dogs. The M.R C investigators examined four other means of flour improvement—chlorine dioxide, potassium bromate, ascorbic acid, and an aeration process—and though these methods were found to have different effects on flour, the evidence was insufficient to call for the abandonment of any of them These methods are to be kept under close scrutiny Presumably millers will use one of the four in place of agene

The facts included in the Minister's statement make us little wiser than we were at the start of 1950 But we can be thankful that the sensible action of banishing the agene process is at last to be taken

## METHYL MERCURY POISONING

THE danger of methyl mercury compounds has been known for nearly a hundred years[4] Such compounds are manufactured in large amounts for the control of agricultural fungus diseases and in 1940 Hunter Bomford and Russell[5] described four cases of poisoning in men engaged in this manufacture. Now fifteen years later one of the four has died and the irrecoverable damage caused by these substances has been described[6]

The destruction proved remarkable for its sharpness and selectivity Circumscribed areas of the visual cortex on the medial surface of the occipital lobes were atrophic and scattered small foci were present elsewhere in the cortex similar sharply defined areas in the depths of some cerebellar folia had lost their granular layer of neurones and secondary changes were present in the glia the Purkinje cells and the superficial layer of fibres the cord and peripheral nerves were not affected These changes account for the clinical signs of great general ataxia and extreme concentric reduction of the visual fields The lesions differ conspicuously from those in the relatively acute stages in the rat and the monkey; here degenerative changes involved the spinal cord and peripheral nerves If this is also the pattern in man it is apparently reversible and the clinical picture indeed suggests that temporary involvement of the nervous system far exceeds the permanent damage

This is the first demonstration in man of primary cerebellar degeneration due to an exogenous toxin and methyl mercury compounds are an important addition to the list of toxic substances with a precise localised effect on the brain The extremely sharp localisation to the depths of particular cerebellar sulci is striking such selectivity is a question sometimes of access sometimes of physiological over use sometimes of a higher organisation and more complex and delicate structure of the cell and its function but none of these explanations seems to apply here, and some chemical difference must be assumed in the affected cells of what to the relatively crude eye of the microscope seems a singularly uniform organ

## FIBRO ADENOSIS AND BREAST CANCER

THE question whether cancer of the breast develops more commonly in patients with fibro adenosis than in other women has never been satisfactorily answered With the intention of settling it Dr William Kiaer[1] has examined 700 breasts from necropsy specimens obtained from women who, during life made no complaint of their breasts and in 33% of this series found histological evidence of fibro adenosis In the 700 breasts examined only 1 case of carcinoma was discovered and he concludes that unlike carcinoma of the prostate latent carcinoma of the breast must be very rare From a study of this material he divided fibro adenosis into three grades, according to the severity of the histological picture Next he made a histological study of 378 breasts in which there was a cancer and 58% of these were found to have fibro adenosis elsewhere The association was particularly distinct with the intraduct type of cancer furthermore it was the grade III (or severest) type of fibro adenosis that was found most often in these cases, and in many a morphological transition from grade III fibro-adenosis to breast cancer was observed microscopically The fibro-adenotic changes were found to be more pronounced in the region of the breast adjacent to the cancer

A further 334 cases of fibro adenosis were examined from the clinical point of view The age distribution showed a peak between 35 and 49 years and the *left* breast was found to be affected more commonly than the *right* *The menopause occurred earlier in this series* than in the normal Where histological control was available it was found that when the patient complained of a discharge from the nipple this was associated with a more severe grade of fibro-adenosis There was no relation between pain in the breast and the grade of fibro adenosis—pain being Dr Kiaer believes, an expression of the fibrosis Of these 334 patients 321 were followed up to see whether cancer developed more commonly in them than in the general population Dr Kiaer refers to Bloodgood's change of heart on this matter which he regards as typical when Bloodgood was a histologist he thought that fibro adenosis frequently led to cancer but when he became a clinician he realised that this relation was far less obvious than histological evidence would suggest Of the 321 patients who were followed up 17 were watched for less than five years 41 for between five and ten years and 203 for more than ten years 21 (6 5%) developed carcinoma of the breast during the period of follow up Histological evidence showed that the higher grades of fibro adenosis particularly grade III were especially likely to lead to cancer and furthermore excision of the grossly affected area did not confer protection Dr Kiaer is aware of the objection that his grade-III fibro-adenosis may be a form of cancer; but he thinks that this is very unlikely because the latent period between the complaint of the symptoms of fibro-adenosis and the appearance of the

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1 Mellanby E. *Brit med J* 1946 ii 885.
2 See *Lancet* 1955 i 81
3 *Ibid* 1950 i [illegible]
4 Edwards G N *St Bart's Hosp Rep* 1865 i 141 *Ibid* 1866 ii, 211
5 Hunter, D Bomford R R Russell D S *Quart J Med* 1940 9 193.
6 Hunter D Russell D S *J Neurol Psychiat* 1954 17 235

1 Relation of Fibro-adenomatosis ("Chronic Mastitis") to Cancer of the Breast Copenhagen: Munksgaard 1954 Pp 169 D kr 30

cancer was generally so long and because many of his cases of grade III fibro adenosis never developed a metastasising lesion

The whole series is analysed statistically by Arne Nielsen, an actuary from the Danish cancer registry, who concludes that breast cancer is 4–5 times as common in patients with fibro adenosis as in the normal population Whether or not this estimate is correct, it seems clear that there is some increased tendency for cancer to develop in patients with fibro adenosis

## RECOGNITION OF TABLETS

We recently *referred to the difficulty of identifying* medicinal tablets [1] This may sometimes be a vital matter, as when an almost empty tablet-box is found beside an unconscious patient Cooper [2] has devised a series of simple chemical screening tests by which many common drugs can be quickly recognised Six reagent solutions are required A few milligrammes of the tablet material is powdered and placed in small heaps on filter-paper A drop of test solution is added to each heap of drug and any colour change is noted By reference to a chart the drug can usually be identified or allocated to a small group If the solutions are already prepared the test takes ten minutes This is an important step forward But it might be objected that the tests, although they have been "streamlined," require time, care, and some apparatus, that the reagents do not keep long and at least some of them may have to be prepared fresh for each test, and that the procedure is inadequate for identifying compound tablets Ideally the responsibility for ensuring that tablets are readily identifiable should rest with the maker Perhaps manufacturers should consider stamping each tablet with an agreed code-number

## TUBERCULOUS PLEURAL EFFUSIONS

Tuberculous pleurisy may seem at the time a short-lived, though uncomfortable, illness But in many patients manifest pulmonary tuberculosis develops later Estimates of the proportion vary,[3] but apparently 20–30% will require further treatment in the next five years The pleural effusion is commonly a gross manifestation of small lung lesions These may not be apparent in the ordinary chest radiographs, but tomography is said to reveal them in about 12% of cases [4] The future of the patient depends on the behaviour of these lesions rather than of the pleura

Long rest and protracted convalescence are usually recommended, but there seems some doubt whether this reduces materially the risk of breakdown Mitchell [5] studied 186 patients treated with varying periods of rest in bed The rate of breakdown in the first five years was 22% among those rested in bed for less than three months and 19% in those rested for longer than six months Emerson [3] found that in 22% of a group of young adults who had had pleural effusions further manifestations of tuberculosis developed in the first two years, even though they had had three months' complete rest in bed He points out that the mean morbidity-rate in the many previously reported series is 30% for those treated with long continued rest and 29 9% for those treated without this

Mackay-Dick and Rothnie [4] advocate repeated aspiration of the effusion and breathing exercises, in order to reduce the risk of later respiratory impairment They claim that the effusion disappears more quickly, but their evidence is not entirely convincing Even if this claim is correct, there is no evidence that the duration of the effusion influences the degree of respiratory disability In any event, it is rare to find any serious disability at all, and the pleura seems to have an astonishing ability to heal It is undoubtedly more important to try and prevent pulmonary relapse, and Mackay Dick recommends treating all patients for six months with antibacterial drugs There is much to be said for protracted drug treatment, and possibly six months is not enough There are, however, arguments against even six months' treatment Some might maintain that it is better to keep the patient under close observation and administer drugs promptly to the 30% who relapse, thereby sparing the remaining 70% the disadvantages of protracted drug therapy It is theoretically possible that the bacilli may become resistant to the drugs during the initial course, and treatment of subsequent relapses will accordingly be less effective, thus although few patients may relapse the same number may die of the disease or have long illnesses Indeed, it is not even known whether antibacterial treatment reduces relapses This would not have been difficult to establish by a controlled trial in the early days of drug treatment, but such a trial would now be difficult and might be unjustifiable Most physicians will probably prefer to judge each case individually

## RABIES IN GERMANY

An epizootic of rabies, described as more serious than any in Western Europe for at least a century, has been spreading westwards across Germany and now threatens neighbouring countries It was discussed at a recent meeting of the Public Health Committee of the Brussels Treaty Organisation [1]

After the first world war, infected dogs, wolves, and foxes from the east caused an outbreak on the eastern borders of Germany This reached a peak in 1924, but veterinary police measures thereafter kept infection beyond the frontiers until the second world war, when it again increased The disease seems to have been prevalent in Eastern Germany from 1945, particularly in foxes and wolves, which could not be shot because the people lacked firearms By 1948 the epizootic had passed the Schleswig Holstein border in the north and reached Austria in the south, and had passed from foxes to dogs, though it preserved its essential difference from earlier outbreaks—namely, the infection of wild rather than domestic animals [2] In 1951 Eastern Bavaria was infected and by last spring large areas from the Danish frontier to Hesse, and some districts bordering the Dutch and Belgian frontiers, were declared infected or suspected Thus in about ten years the epizootic has spread stealthily right across Germany, though most of *the southern parts of Western Germany remain free*

Though the disease is more easily detected in domestic than wild animals, two thirds of the material diagnosed as rabies in the government veterinary laboratories have *come from wild animals* (foxes, badgers, roe deer, hares, rabbits, weasels, wild boars squirrels, rats, buzzards, and magpies) cats, dogs, cattle, and other domestic animals have provided the remainder, though in herbivores infection is rare Incidence is highest in winter and spring, and rivers seem to be no obstacle to spread The chief diagnostic signs are the well known changes in behaviour Thus foxes lose their fear of man and may be seen walking in a village street they have even allowed themselves to be picked up by children Refusal of food, and biting of inanimate objects are characteristic as are changes in voice Buzzards, in which Negri bodies were afterwards found, have dashed themselves to death against windows In material from animals in which rabies has been clinically confirmed, Negri bodies have been found in about 75% [3] In addition, the intracerebral and intramuscular injection of suspect material into white mice is employed

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[1] See *Lancet*, 1954 ii, 697
[2] Cooper, P *Pharm J* 1954, 173 481
[3] Emerson P A *Brit J Tuberc* 1954 48 261
[4] Mackay-Dick J Rothnie, N G *Tubercle* 1954 35, 182
chell R S *Amer Rev Tuberc* 1953 67 421

[1] Netherlands report to the Public Health Committee of the Brussels Treaty Organisation Unpublished
[2] Zunker M *Bull Off int Epiz* 1954, 42, 83
[3] Ruppert F *Ibid*, p 70

Only one case of human rabies has occurred in Western Germany, but the number of people vaccinated is large and rapidly increasing—i e 423 in 1953 and 828 up to June 5 1954 the greater part from Lower Saxony North Rhine Westphalia and Hesse Vaccination is recommended for all who have been bitten scratched, or licked by infected or suspected animals who have handled them, or who have been in contact with their saliva (e g on muzzles or pieces of wood) No cases of postvaccinal paralysis are reported and hyperimmune serum has not been employed

The basic control measures are first notification secondly destruction of foxes and badgers by shooting and cyanide fumigation of the earths and thirdly declaration of infected or suspected areas. In such areas dogs must be kept tied up for three months and cats kept at home any found at large are shot and since sooner or later a cat will walk by itself,' most cats in these areas have been killed Energetic measures against foxes—3000 have been destroyed in the province of Detmold (North Rhine Westphalia) in eight months—seem to have been effective in stopping the epizootic Education of the public is regarded as very important [4] It is noteworthy that vaccination of dogs has been rejected as a control measure on the grounds that (a) wild animals are chiefly affected (b) cats are considered more dangerous than dogs ; (c) police measures have been successful in the past in controlling infection in dogs (d) vaccinated dogs must still be controlled because their saliva is infectious even though they are protected against clinical development of the disease ; (e) the public would be less likely to coöperate in other control measures if dogs were vaccinated and (f) the cost and effort in vaccinating all dogs would be very great For these reasons the vaccination campaigns such as have been successful in Hungary Japan Israel and Malaya [5] are not thought to be applicable to conditions in Western Germany

Denmark has so far remained entirely free, thanks perhaps to destruction of foxes along the frontier and mass vaccination of dogs in frontier areas It seems unlikely however that such measures will stop the epizootic from crossing the long western frontier of Germany

For us the moral is clear Quarantine has fallen into disuse as a prophylactic measure against many diseases, but against animal rabies it remains our great protection Anyone smuggling in a dog from Western Germany commits not only an offence but a serious crime against the canine—and perhaps the human—population in this country

## ANTIGENICITY OF COLLAGEN

AMONG connective tissue diseases rheumatic fever has always seemed to have the best claim to an immunological origin Yet although the evidence implicating the group A hæmolytic streptococcus is strong no particular bacterial antigen or antibody has been identified as a specific causal factor Alternatively the antigen may lie in or be derived from the connective tissue itself and auto antibodies may be the cause of lesions involving among other possible components collagen Hitherto collagen (which is by bulk the chief component of connective tissue) has been thought to be non antigenic as is its soluble derivative gelatin and its immunological harmlessness is presumed in its use (in a somewhat modified form) as surgical catgut Reticulin however which in some ways resembles collagen probably has immunological activity the work of Hill and Cruickshank [6] on fluorescein labelled tissue antibody strongly suggests that the antigenic component in kidney glomeruli, for example, is reticulin

Evidence is now forthcoming that soluble collagen is also antigenic Watson et al [7] have prepared acetic acid extracts of rat tail tendon with special care to prevent denaturation and have immunised rabbits by intraperitoneal infusion of the extracts After somewhat prolonged immunisation some of the rabbits produced antibody giving specific complement-fixation results with the immunising solution Their experiments are designed to meet the criticism that the antibody produced is not specifically directed towards collagen but to an accompanying impurity and their results justify their conclusion that they have obtained an antiserum specific for the acetic acid soluble component of collagen Particularly striking is their demonstration that whereas the addition of normal rabbit-serum to the acid-collagen solution led to the reconstitution of fibres which sometimes showed the characteristic collagen periodicity in electron micrographs the addition of the specific rabbit-antiserum gave rise instead to a globular form of precipitate which never included fibres with periodic banding They also describe evidence (and this if confirmed is another important new finding) that collagen exhibits species specificity

These results clearly hold promise of an effective method of investigating connective-tissue reactions to specific antibody

## PRIVATE ADVENTURE MONEY

SINCE it was founded in 1943 the Nuffield Foundation has allocated grants of over £5 million and with its annual report for 1953–54 [8] it publishes a full survey [9] of all the grants made during its first ten years These reports appear at a moment when the great American foundations face Congressional criticism. Like their creators the Carnegie Rockefeller and Ford Foundations are big enough to speak for themselves but their generosity has been international and British scientists can gratefully apply to them all the words Dean Rusk has written about the Rockefeller Foundation

> As a social institution it reflects the application to philanthropy of the principles of private initiative and free enterprise, under public policies which have long recognized the benefits of such activity to a free society [10]

Though research education and welfare services in this country receive more and more help from the State there is still plenty of room here for imaginative experiment But in some of the other countries of the Commonwealth the gaps are even more conspicuous and in the past few years the Nuffield Foundation has accordingly given more private adventure money " to people and institutions in overseas parts of the Commonwealth One of the most important of these allocations has been grants of £250 000 to university colleges in Colonial territories This generous help will give the foundation a particular pleasure which we all share, in the announcement last month that the University of London has confirmed the conferment of M B B.S degrees on thirteen students of the University College of the West Indies who passed their final examinations in October

As one quinquennium ends the next begins and the report also outlines the foundation s plans for the next five years. As its special interest in medicine it has chosen the investigation of the chronic rheumatic diseases and the causes of mental and physical defects which throw so heavy a burden on the family and the community ' It also shares Professor Adrian s belief in the importance of the development of the social sciences, and it hopes to encourage fundamental research into such subjects as the family For instance, Belmont Hospital, Surrey, over three years, is to receive up to £19,500 for a study of the family and social background of some patients in the unit lately described in our columns by Dr Maxwell Jones[11] The foundation's interest in the problems of old people is of long standing, and here it hopes especially to help in research and practical experiment in the employment of elderly workers

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[4] Bull World Hlth Org 1954 10 618
[5] Tech Rep Wld Hlth Org no 82 April 1954
[6] Cruickshank, B., Hill A G S In Nature and Structure of Collagen Edited by J T Randall London 1953 p 77
[7] Watson R. F Rothbard, S Vanamee P J exp Med 1954 99 535
[8] Nuffield Foundation Ninth report 1954 Pp 141
[9] Nuffield Foundation Report on Grants 1943–53 Pp 319 Both obtainable from the Foundation Nuffield Lodge Regent's Park London N W 1
[10] Rockefeller Foundation Annual Report 1953. President's Review p 8

## ULTRASONIC IRRADIATION OF THE FRONTAL LOBES

THE effects of ultrasonic waves on biological systems have interested experimentalists for nearly thirty years In the past ten years they have been used to damage various parts of the brain in living animals Lynn and Putnam[12] found that neurones were more severely affected than glial cells, and that blood-vessels suffered least In their experiments the scalp and skull were not opened, and radiation intense enough to harm the brain caused also dry gangrene of the superficial tissues The mode of production of lesions is obscure The absorption of ultrasonic energy by homogeneous liquids is not fully understood, and conditions in the brain must be even more complex

In what appears to be the first report of the use of ultrasonic energy in neurosurgical practice, Lindstrom[13] describes its effect in twenty cases in which the prefrontal lobes were irradiated—in seventeen cases of malignant disease for relief of intractable pain, and in three cases of organic nervous disease with psychiatric complications Preliminary trials in rabbits showed that the cerebral effects were uselessly variable unless the scalp and skull were opened

In dogs and rabbits it seemed to matter little whether the dura also was reflected The transmitting quartz crystal, 1¹/₄ inches in diameter, oscillated at 1000 kc per second The waves were conducted to the brain through Ringer's solution percolating through a plastic cup, either cylindrical, or conical to focus the beam Maximum energy was estimated to be 7 watts per cm² cross section area of beam near the crystal. The aluminium face of the oil filled crystal container was separated from the brain by 1 5–4 0 cm of Ringer s solution In the animal brains lesions were found mainly in the white matter, following especially the contours of its junction with the over lying grey, which was often apparently unharmed

In patients 1¹/₄–1¹/₂ inch buttons of bone were removed from the frontal bone, 1 cm in front of the coronal suture and in line with each pupil The beam was aimed in the direction of the tip of the anterior horn of the ventricle on each side Exposure time was four to seven minutes with dura open seven to fourteen minutes with dura intact Fourteen of the brains were later obtained for anatomical study, when the lesions were between nineteen days and seven months old Detailed descriptions are promised later

Macroscopically, most brains appeared normal Microscopically the inconspicuous cortical damage was consistent with the use of diathermic coagulation for dural bleeding Scattered small foci of gliosis were found in the white matter, especially near its junction with the cortex, near blood vessels, and near the tip of the ventricle Yet, notwithstanding the relatively slight structural changes, ten of the seventeen patients with painful malignant disease were completely relieved, and four more were partly relieved, of their complaints

The indications for destructive operations on the frontal lobes will continue to be debated All parties to the debate will need to take this new method into account It is not too much to ask that no neurosurgeon should use it on his patients without having standardised the performance of his apparatus experimentally The ultrasonic method does seem to offer new possibilities of inflicting damage which, presumably maximal at first, may be partly reversible, so that the permanent damage is very much less than that caused by s lobotomy If further clinical and pathological experience confirms the results in this small series, will it not suggest the possibility that temporary lesions may break up, for example, some habitual mental attitude, and that this need not return when neuronal structure and function are later partly restored ?

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[11] *Lancet* 1954 ii 1277

[12] Lynn J G Putnam T J *Amer J Path.* 1944 20 637

[13] Lindstrom P A *Arch Neurol Psychiat* 1954 72 399

## LYMPHŒDEMA PRÆCOX

THE lymphatic circulation, carried as it is in fine transparent vessels, has been largely neglected by clinical investigators, other than those interested in cancer dissemination This is due partly to the difficulty of displaying lymph-vessels and partly to the lack of an adequate clinical method for determining their functional efficiency Kinmonth[1] has reviewed some of the methods at present in use

Patent-blue V is a convenient dye for the study of lymphatic pathways, and can safely be injected into the subcutaneous or deeper tissues "Streamers" of dye-filled lymphatics can be seen to leave the injection site, and massage or limb movement forces the dye into the regional lymph nodes The blue tinge following superficial injection disappears in forty-eight hours Kinmonth has shown that dye injected into the interdigital spaces of the normal foot or hand is quickly demonstrable in the groin or axilla, and similarly it will outline the lymphatics in the spermatic cord, breast, or mesentery. Sometimes a lymphatic revealed by patent blue V has been successfully dissected out and injected with a radio-opaque material, such as diodone

In the normal limb the diameter of the lymphatic trunks, which anastomose and bifurcate as they approach the root of the limb, remains relatively uniform But in lymphœdema præcox[2] the lymphatics in half the patients are tortuous, dilated, and incompetent They are valveless and may be reasonably compared to varicose veins, and dye techniques have revealed incompetence of the deep lymphatics in addition to the well recognised superficial lymphatic abnormality Jepson et al.[3] attempted to assess the removal rate of tissue-fluid and thereby lymphatic efficiency, by estimating the absorption of radioactive protein, and Kinmonth[1] has applied this technique to lymphœdematous limbs, and suggests that in these dispersion of the tagged protein is slower than normal Analysis of tissue fluid in lymphœdema reveals high levels of protein, except in cases of chylous reflux when the œdema fluid has a high fat content

These findings in the lymphœdematous limb should be kept in mind when the question of operation arises. An operation designed to repair the anatomical and functional defect seems to be out of the question, since both deep and superficial lymphatics are at fault, the introduction of valved lymphatics by a skin bridge from the abdomen to the thigh only nibbles at the problem. Apparently the surgeon must rely on excisional surgery by which the œdematous subcutaneous tissue is radically excised and the leg shaped for cosmetic effect Development in skin grafting methods—for example, the use of the electric dermatome—have greatly simplified skin replacement But such major operations, which are often associated with considerable blood loss, must be kept for the occasional case where the leg is so huge that it handicaps the patient mechanically

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Prof ROBERT CRUICKSHANK has been appointed principal of the Wright-Fleming Institute of Microbiology in succession to Sir Alexander Fleming, F.R.S., who has retired Professor Cruickshank will continue to hold the chair of bacteriology in St Mary's Hospital Medical School

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[1] Kinmonth J B *Ann R Coll Surg Engl* 1954, 15, 300

[2] See *Lancet*, 1954 i 766

[3] Jepson R P Simeone, F A Dobyns B M *Amer J Phys* 1953 175 443

# Special Articles

## OBSTETRICS AND PSYCHIATRY *

G R HARGREAVES
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CHIEF OF THE MENTAL HEALTH SECTION WORLD HEALTH ORGANISATION

OBSTETRICS has the unique distinction of being the only branch of clinical medicine which concerns itself predominantly with healthy human beings, and occupies itself principally with assisting a physiological process rather than with interrupting one which is pathological Psychiatrists, on the other hand, are generally assumed to devote their interest to patients whose symptoms make them appear so remote from their fellow human beings that they are thought of as *aliénés*; a psychiatrist, at any rate in the eyes of those who call him an alienist appears to occupy himself with 'foreigners, which means, as every Englishman knows, people who are far from normal

When I say that nevertheless obstetrics and psychiatry share an important area of common interest I am not referring merely to the puerperal psychoses. The puerperal psychoses are to the psychiatrist important chiefly as the presenting symptom of a much larger group of psychological problems associated with childbirth which like the main bulk of an iceberg are not so easily visible (Indeed psychiatrists would suggest that the only thing common to the psychoses of the puerperium is the fact that they occur during the period after childbirth for they include almost every type of psychosis which may occur at any time of life ) The psychoses arising in childbirth or any other situation are outnumbered, at any rate in the Western countries by the psychoneuroses

The fact that this is still little recognised by physicians who are not psychiatrists arises partly from the deficiency in this respect of most current medical education but also from the fact that the manifestations of a neurosis are little evident to the observer and may easily be ignored by everyone except of course the patient whereas the destruction of the personality which accompanies a psychotic illness leads to disturbances of behaviour which even the most obtuse observer will perceive

But whether a patient be suffering from the comparatively rare condition of psychosis or the far more common one of psychoneurosis the psychiatrist as he takes his history cannot fail to be impressed by the frequency with which he finds the occurrence of pregnancy and birth as one of the ætiological threads in the weaving of the illness whether it be the pregnancy of the patient herself or the pregnancy or birth of others intimately involved in the patient s life situation

### STRESS

Whereas it was formerly supposed that mental illness was hereditary we would now prefer to say that what is inherited is not the illness but the possibility of developing it Whether a person who inherits this possibility does in fact develop the disorder depends on the emotional stresses of his life experience and his reaction to these stresses depends partly on the experiences themselves and perhaps partly also on another hereditary factor of general resistance—of capacity to adapt constructively to such emotional stresses

Emotional stress, in the sense of the psychiatrist, can best be considered as a sudden demand on the individual for adaptation to a radically changed pattern of human relationships and the capacity to react to this change is influenced by past relationships all the way back to childhood In this respect there is no change more drastic in its effects on all within the immediate family circle than the birth of a new human being The emotional stresses with which the psychiatrists are concerned in the ætiology of psychiatric disorders are not hurricanes floods, wars and the other relatively rare cataclysms which the insurance companies refer to as 'acts of God' but the emotional stresses of adaptation to those suddenly and radically changed intimate relationships which, far from being rare are the inevitable lot of every human being

It will be evident that by far the most important agents of emotional stress in this sense are the ubiquitous phenomena of birth and death Because of this, all human societies from the dawn of history have evolved ceremonies and rituals to support their members through the stress of emotional adaptation which the beginning or the ending of a life imposes upon others and the stresses which arise at all those steps on the path between the beginning and the end in which the individual s relationships are suddenly and drastically changed Birth ceremonies, puberty rituals, initiation procedures marriage ceremonials, and burial rites are in fact the intuitively devised prophylactic measures by which societies temper the emotional winds that blow on those suddenly shorn of old relationships or forced to adapt to new ones In our sophisticated Western cultures these ceremonies tend to wilt under our scientific criticism of what we call superstition—and so we are left with the stresses but no communal mechanisms for helping us to adapt to them —unless like the *Times* with its obstinate and conservative sense of reality we can remember in our clinical practice that births deaths and marriages are front page news for the individual human being, and that politics and international affairs can wait until p 8

### RÔLE OF THE OBSTETRICIAN

Our Western societies have demanded of the obstetrician the utilitarian function of preventing death in childbirth and since the days of Semmelweis the obstetrician has lived up to this expectation with a success to which the maternal mortality rates of the Western world bear ample witness But the original social function of the folk midwife of a primitive tribe was I suspect, probably not that of the scientific obstetrician—to protect the woman and her child from death in childbirth—but rather to support the mother and her family through the processes of psychological adaptation demanded by a new birth Even this more modest function however may well have made its indirect contribution to the far more difficult tasks of modern obstetrics when we remember the extraordinary rarity in primitive peoples of primary uterine inertia, or failure of lactation—those two bugbears of Western obstetric practice

The Western science of obstetrics has excelled in the new function of the prevention of death; and yet perhaps in doing so at any rate in the half-century which has recently passed it has tended to forget the emotional needs of the mothers and babies who lived It is immensely to the credit of the specialty that the balance is now so rapidly being redressed and that some obstetricians having brought under control the physical hazards of childbirth are now turning their attention to the psychological stresses it entails

The current interest in the training of the pregnant woman for active participation in childbirth the development of rooming in ' and of self-demand feeding practices show that the obstetrician having relegated death to the position of a minor risk in childbirth is capable of continuing to develop his function of helper in a normal biological process by fostering the psychological readaptation for which that process calls

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* From a paper read to the International Congress of Obstetrics and Gynæcology Geneva July 1954

### RÔLE OF THE PSYCHIATRIST

"But where," you may ask, "does the psychiatrist come into all this?" To which I can only reply "He comes in too late" He sees the end results of the failure of that adaptive psychological process—and he sees them at a time when the failures are consolidated in the form of an established neurosis or psychosis, when only extensive therapeutic endeavour can change the picture Yet it is evident to him that, before that state arose, in every patient's case there was a period of fluidity, of plasticity, when very simple measures might have tipped the scale in the opposite direction This was the period during which pregnancy and the birth of a child first threw on the family constellation a demand for psychological adaptation to which it finally failed to respond constructively At this period it is not the psychiatrist but the obstetrician and the obstetric nurse who have the opportunity for action, but perhaps the psychiatrist can help to train them to make the best of this opportunity

He can tell them something of the normal anxieties and psychological preoccupations of pregnancy, the deep archaic fears that are stirred by this primitive biological experience fears which seem worlds away, or perhaps I should say centuries away, from the everyday life of the Western world The idea of the "evil eye," for instance, so long ago discarded as a superstition in our societies, feels like a reality at some time or other to many pregnant women Mood changes that affect temporarily, but deeply, the woman's attitudes to her husband or her unborn child Her gruesome fears about her own body or that of her unborn baby All these are among the normal abnormal thoughts of many pregnant women

Ignorance of the natural history of the psychological aspects of maternity also causes problems for many a woman who suffers unnecessary anguish and sometimes a permanent twist of attitude as the result of the latent period of absence of feeling for her newborn child—not knowing how normal this is, and that within a few days or weeks her motherly feelings towards her infant will suddenly mature with overwhelming force

The psychiatrist can also offer to the obstetric worker techniques for resolving or dissipating such anxieties It is heartening to see that the skills developed by the psychiatrist in the field of group psychotherapy are beginning to be used by obstetric workers in therapeutic discussion groups for pregnant women and young mothers in which these normal archaic anxieties to which I have referred can be worked through

At this point some one might interject "Why bother? The average woman and her husband cope with the psychological readaptation to childbirth without our aid" To which the psychiatrist would be tempted to retort a trifle tartly that the same is probably true of the physical hazards of childbirth, and that, in the one field as in the other, it is during the antenatal period that we must try to discern those whose risk, either physical or psychological, is greater than the average Certainly some pregnancies raise greater psychological problems than others, either by virtue of the woman's previous experience of a pregnancy that ended in catastrophe, or —even more serious—where it was secretly self-terminated Most dangerous of all is probably the pregnancy which the woman failed to terminate Her previous personality is an equally significant factor The identification in the antenatal clinic of a woman with a markedly immature, dependent, and infantile personality is perhaps therefore as relevant a part of the antenatal examination of the future as the recognition of a contracted pelvis was in the past, both call for special antenatal prophylactic measures

All this, from the psychiatrist's point of view, is important enough with the birth of a normal infant, but it becomes doubly so with a dead baby or an abnc child A woman who has invested the emotions of nine months' pregnancy and a labour in what proves to be an abnormal child, is from a psychological standpoint, in great danger—and yet, at the same time, much more accessible to help than she will be six months later The person who can most easily help her, by virtue of her existing relationship with her, is her obstetrician Therapeutic discussion at this point may change the whole future development of the child by preventing the mother's relationship with him being wrecked on the scylla of rejection or the charybdis of guilt ridden overprotection

The obstetrician and psychiatrist have, I believe, a duty to collaborate to ensure that obstetricians of the future are well equipped, by the training we give them, to cover this new, and yet very old, aspect of their specialty

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## SWEEP-FREQUENCY METHOD OF TESTING THE HEARING OF SCHOOL-CHILDREN

THE following statement has been prepared by Prof. A W G **EWING** at the request of the Medical Research Council's Committee on the Educational Treatment of Deafness

In a recent investigation it was found that approximately 70% of pupils in English schools for the deaf and partially deaf have suffered from their handicap since before the age of two years From the Ministry of Education's returns and from the results of recent surveys it seems that nearly all deaf children are admitted to special schools by the age of seven years, but that the ascertainment of partial deafness as a cause of educational retardation is at present less effective among children under seven than among those who are older

The sweep frequency technique has been shown to be a reliable and efficient method of making screening tests of the hearing of five and six year old school children A pure-tone audiometer is used and, when the range of frequencies that are used is extended from 250 to 6000 cycles per second early symptoms both of conductive and of perceptive deafness can be detected It has been established that a sweep check over this range of frequencies at 15 decibels above normal threshold of detectability is more thorough and reliable as a screening test than the use of word material (as in the test by gramophone audiometer) the loudness of which cannot be monitored satisfactorily for this purpose The fading intensities, called number test has been shown to be sometimes ineffective for the detection of high tone deafness

Audiometricians who have been trained to work with young children are able to make a sweep check of auditory acuity, as an individual test, at a rate of three minutes per child It has been shown that extraneous noise in a room in which a screening test of hearing is to be made should not exceed about 30 decibels The sweep frequency test can be made in a small room. When it is necessary to make screening tests of children's hearing in school buildings it is much less difficult to find small rooms that are quiet, in schools, than large rooms

The sweep frequency test can be made immediately or soon after children are first admitted to school, whereas the gramophone audiometer test, as normally administered, is a group test, in which children are required to write down numbers that they hear It cannot therefore be used with children younger than eight years The sweep frequency test is very valuable in screening out children who are likely to need hearing aids and special educational treatment before they have been exposed to the risk of educational subnormality as a result of defective hearing

A comparative study of the relative reliability of the sweep frequency and gramophone audiometer tests, when both were administered to six year old children individually, showed the sweep frequency tests to be superior The called numbers that are used in the gramophone audiometer test involve a constrained context and are therefore often recognisable by children suffering from loss of hearing to a significant degree

## HOSPITAL COSTING

The Hospital Costing Returns for the year ended March 31 1954, have now been published by the Ministry of Health[1] They cover some 2500 hospitals in England and Wales, and are based on the headings of the hospitals financial accounts. The general pattern of the tables is the same as in previous reports but the analysis is even more detailed and the returns from each hospital are now tabulated under some 47 headings A working party set up by the Minister is still deliberating upon a more informative system of costing meanwhile the costs for outpatients continue to be unavoidably included with those for inpatients, and in the calculations five outpatient attendances have again been taken as equivalent to one inpatient day—a questionable assumption as we have already pointed out[2] On the other hand the additional information does allow more just comparison to be drawn between hospitals of equivalent *status*

The accompanying table shows the steady rise over the last four years in the national average costs per week of patients in the main types of hospitals (the figures are adjusted for notional outpatient expenditure and exclude returns from teaching hospitals) For London teaching hospitals classified as general, the average cost (computed on the same basis) was £25 4*s* 2*d* in 1953–54 compared with £24 18*s* 8*d* in 1952–53 Equivalent figures for provincial teaching hospitals were £19 2*s* 9*d* (1953–54) and £18 13*s* 9*d* (1952–53)

HOSPITALS ADMINISTERED BY REGIONAL HOSPITAL BOARDS AND HOSPITAL MANAGEMENT COMMITTEES

| Classification of hospital | Year ended March 31 | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1951 | | | 1952 | | | 1953 | | | 1954 | | |
| | £ | s | d | £ | s | d | £ | s | d. | £ | s | d |
| General | | | | | | | | | | | | |
| 1–50 beds | | | | 12 | 11 | 9 | 13 | 13 | 6 | 14 | 7 | 8 |
| 51–100 beds | | | | 14 | 7 | 2 | 15 | 7 | 5 | 16 | 1 | 3 |
| 101–300 beds | 13 | 10 | 3 | 14 | 13 | 3 | 15 | 10 | 6 | 16 | 2 | 4 |
| 301–900 beds | | | | 14 | 11 | 7 | 15 | 12 | 1 | 15 | 19 | 1 |
| Over 900 beds | | | | 10 | 0 | 10 | 11 | 8 | 11 | 11 | 16 | 3 |
| All hospitals | 13 | 10 | 3 | 14 | 5 | 11 | 15 | 4 | 9 | 15 | 15 | 5 |
| Mainly general | 11 | 12 | 3 | 12 | 10 | 10 | 13 | 4 | 7 | 13 | 16 | 1 |
| Mainly chronic | 6 | 18 | 4 | 7 | 5 | 1 | 7 | 12 | 10 | 8 | 6 | 8 |
| Chronic | 5 | 15 | 5 | 6 | 0 | 0 | 6 | 11 | 6 | 7 | 0 | 2 |
| Convalescent | 6 | 15 | 9 | 6 | 12 | 11 | 7 | 11 | 4 | 8 | 3 | 0 |
| Isolation | 16 | 11 | 1 | 17 | 0 | 1 | 17 | 0 | 0 | 19 | 0 | [illegible] |
| Maternity | 16 | 9 | 6 | 16 | 19 | 2 | 17 | 13 | 1 | 18 | 0 | 5 |
| Mental | 3 | 15 | 11 | 4 | 1 | 1 | 4 | 8 | 6 | 4 | 12 | 0 |
| Mental deficiency | 3 | 11 | 4 | 3 | 17 | 1 | 4 | 4 | 4 | 4 | 8 | 11 |
| Orthopædic | 9 | 17 | 0 | 10 | 15 | 3 | 11 | 13 | 0 | 12 | 0 | 11 |
| Tuberculosis | 8 | 17 | 2 | 9 | 0 | 7 | 9 | 19 | 6 | 10 | 8 | 1 |
| Tuberculosis and isolation | 12 | 11 | 8 | 13 | 3 | 8 | 13 | 5 | 7 | 14 | 1 | 5 |
| Children (general) | | | | | | | 13 | 17 | 2 | 15 | 6 | 4 |
| Ear nose and throat | | | | | | | 14 | 6 | 4 | 15 | 5 | 2 |
| Eye | | | | | | | 12 | 9 | 3 | 12 | 15 | 4 |
| Eye and ear nose, and throat | | | | | | | 15 | 5 | 1 | 15 | 17 | 11 |

The costs vary considerably with the size of the hospital and with the regional area concerned. Thus in 1953–54 in the North West Metropolitan region the average cost in hospitals of 1–50 beds was £16 17*s* 6*d* per patient per week while in the same region the figure in hospitals with 301–900 beds was £20 9*s* 10*d* Equivalent figures for the Newcastle region were £12 1*s* 3*d* and £15 1*s* 9*d*

The Minister in drawing the attention of hospital authorities to the returns points out that in the past they have proved a useful stimulus to the elimination of extravagances and to the more efficient use of available funds Clearly they will serve their purpose even better when the long awaited improvements in methods of costing are eventually introduced.

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[1] Hospital Costing Returns: Year ended March 31 1954 H.M. Stationery Office 1954 Pp. 173 1s. 6d

[2] See *Lancet* 1953, i, 1013.

# Points of View

## INSTITUTIONAL MEDICINE

*From the Posthumous Papers of*

SIR JAMES SPENCE*

It is I think, one of the inherent peculiarities of an Englishman and more particularly of a Northumbrian that if you scratch him he begins to brood over his *institutions* And *then from time to time he reforms* them. He is, as it were still in the atmosphere of those tremendous years before and after 1688, when our revolution was settled more by sincerity of argument than by force of arms and when there were men of the calibre of Halifax the Trimmer to hold the balance Now again in this century we are in the midst of another revolution which is shown by our concern about our institutions If we have neither the vigour which is an affair of the spirit, nor the means which is an affair of the intelligence to reform our institutions it will be a matter of interest mainly to the historians of the future but such a state of affairs will be cold comfort to those of us who believe that the excellence of civilisation is shown in the capacity of its citizens constantly to reform its institutions in order to meet its changing cultural needs. But change may be for the better or the worse, and in remembering this we should be guided also by Burke s admonition that merely to innovate is not to reform '

To be an institution means many things but on the whole the word has now a derogatory meaning It conjures up pictures of buildings and committee rooms of barracks and corridors of orphanages and museums and to call someone an 'institutional child is to speak half in pity and half in reproach I will try to refresh the meaning of the word by reminding you that an institution is people and not things An institution is the establishment and arrangement of human effort towards a common end It will stand or fall according to the value of this end, or purpose as we may call it and according to the means which are used to reach it The means are the government the administration and the arrangement for carrying out its work—three quite separate functions which must not be confused As the end never justifies the means, so these means or functions are all important By these standards most institutions neither stand nor fall but just flounder along because their end is forgotten or because their means are confused or inept You must forgive my presumption in placing these elementary thoughts in your minds before turning to the profession and practice of medicine which is now so involved in institutions that I must attempt to find a way through their maze

Seeking definitions for the foundation of an argument like this I go back to that early arch Englishman Thomas Hobbes—who was rare at definitions In discussing how the liberty of subjects is to be measured, he stresses the overriding need for government or sovereignty as he calls it and distinguishes between Sovereignty by Acquisition and Sovereignty by Institution The former is to govern through the seizure of power the latter is to govern by the covenant of one to another or of the many to the few This definition gives to the word institution the meaning I wish to convey Institution is to covenant that something shall be carried out and to transmit to someone the authority to arrange for it to be carried out I shall accept this definition when I mention the institutions which affect medicine and the disorders which beset them

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* The opening passages of the presidential address given by the late Sir James Spence to the Newcastle upon Tyne and Northern Counties Medical Society in October 1953 followed by an outline of the rest of the lecture prepared from Sir James's notes

I have indicated that institutions may be good or bad, or good in parts, or just floundering along If they are bad there are usually three possible causes These are (1) that they do not know or see clearly what they are trying to do—or there are conflicts of purpose in what they are trying to do , (2) that they have not the will to do what they know they should do (which is a fault of government) , and (3) that they do not have the ways, and kind of people, to do what they want to do (which is a fault of arrangement or administration) Where arrangement or administration fails it is usually because there has been no clear definition of responsibility

The simpler the institution, and the clearer its purpose, the easier it is for it to be successful At one end of the scale we have simple institutions, like football teams, cricket clubs, ships' crews, and public schools, whose purposes are clear, and in which the division of responsibility is precise under arrangements which can be judged by results At the other end of the scale we see complicated institutions like trade unions, professional associations, regional boards, trade corporations, national coal boards, and city councils If they fail or flounder it is because their purpose is not clear or because their government and arrangement do not match their purpose

[Here the lecturer spoke of the definitive distinction between a service and an institution ]

I can go no further in this attempt to anatomise human institutions, but before I look at the institutions which affect medicine I will recapitulate in mentioning three aspects of them which may be worth bearing in mind

The first is the great increase in number and size of institutions in recent years This carries the danger that we are creating institutions beyond the capacity of the available intelligence, the available will, and the available morality which are necessary to maintain them

The second point, which arises from the first, is that the creation and maintenance of complicated institutions demand a particular kind of intelligence, personality, and education in those responsible for them The form of this education took shape in John Locke's famous essay, and the substance of it was given in our older universities, at a time when they were designed to give an education for responsibility This education was reinforced by a system in which the younger men knew intimately the older men experienced in the art of government In the aristocratic tradition this was still further strengthened by the concept of *noblesse oblige* If we were to seek modern examples of these mature craftsmen in the art of government of human institutions we could use John Anderson in our own day, and Robert Morant before him , but the weakness of our present situation is that it is impossible for a sufficient number of people to get close enough to men like Anderson and Morant to learn from their examples

The third point concerns the manners of those who take part in the affairs of institutions and by manners I mean *mores*, and therefore morality It is beyond question that the manner, or morality, of most of us towards a simple institution like our family or our cricket club tends to be of a different order from that we adopt towards complicated and impersonal institutions like British Railways or the Commissioners of Income Tax An appropriate morality is achieved satisfactorily in a good naval vessel, a good battalion, and a good university , but in the vast impersonal social institutions we are now creating the very opposite may happen Perhaps our fate is that our civilisation will flounder in the midst of the vast institutions it builds, but which it cannot maintain, for want of capable men They will then be like the dinosaurs—too big for their jobs, or too big for their shoes

* * *

There was need, Sir James continued, for careful study of the defects and disorders of the many kinds of institutions affecting the profession and practices of medicine—for the study of *clinical institutology*, or the morbid anatomy of medical institutions

Explaining what he meant by *medicine*, he described it as the fulfilment of a social contract or covenant between a professional man and another man who is sick or who fears he is sick The fulfilment of this contract was in giving advice, explanation, or treatment, or any combination of these The contract might be with a group of professional men, but in that case there was clear division of responsibility Personal responsibility was the essence of medicine—the patient goes to a doctor not to a board of governors or a clinical cure company—and the doctor's first responsibility was to his patient not to his employer

### *Types of Institution*

Among the institutions affecting medicine two kinds of *professional association* could be distinguished (a) those which are simply medical societies, and (b) those which have power over other people, such as the Royal Colleges with their diplomas and the specialist societies in America

Of these the *medical societies* came first, for many reasons Of all medical institutions they were the most moral—in purpose, in method of government, and in method of administration They had frailties rather than disorders, and these were all in the officers rather than the members

A third type of medical institution was *family practice*, whether by a group or by a single doctor Fourth we might have the *health centre*—but not yet He thought this would become a local service rather than an institution

As an example of an institution nearly perfect in type, he described the working of the *Medical Research Council* and its National Institute of Medical Research

Turning finally to the *hospitals*, he spoke of their development in four phases first, the founding phase (round about 1750) , secondly, the period when the hospital was the place of the predominant practitioner (1800–1900) , thirdly, the period when it was the jumping off ground for consultants—when practice was obtained through hospital reputation (1900–1930) , and fourthly the period when it became a centre for specialist services with development of peripheral specialist units

Of hospital problems, the first was size a hospital of up to 150–200 beds could be an institution, but above that size it was likely to become a service In speaking of organisation, he recalled his definition of institution as the establishment and arrangement of human effort towards a common end, and said that he knew of no example of a good hospital which has not been created through the good offices and good will of its medical staff Occasionally one might see a hospital which is very good but in which the medical staff appeared to play very little part in the government , but such a hospital functioned through the excellence of its component institutions It was a fault if the medical staff either cannot or do not give guidance to the governing body

The size and complexity of the large modern hospital made it a service rather than an institution, and much depended on the size of its constituent units The size of the unit in turn depended on the proper size of the team in charge of it, which (he suggested) should not exceed 10–12

The task of the teaching hospital was complicated by its additional responsibility for teaching and research nd here Sir James Spence expressed his regret at the ilure of the concept of the region with a university ospital at its centre *The position of the teaching hos* ital had become precarious through the growth of gional hospitals as specialist centres and through its onsequent loss of acute medicine and surgery and the iseases about which general practitioners most need dvice and help In his opinion it had been a grave istake not to make the teaching hospital a university stitution, giving it a local area in which it would e responsible for designing the entire hospital service t should be a central hospital for acute medicine, surgery nd fevers and with specialist annexes

### *he University Pattern*

Outlining the design of the teaching hospital—its ethodology its morality its style—Sir James Spence rew a parallel with the English university at its best ts three purposes—clinical science clinical teaching nd the care of the sick—were comparable to the three urposes of a university which are to advance scholar hip to teach students and to create a university life nd there need be no conflict between these purposes Ie believed that just as universities are free from the ontrol of the Ministry of Education, so teaching hos itals should be free from the control of the Ministry of Iealth.

In conclusion, he spoke of his faith in the future of ur universities through which England would endure They are big but they remain an institution Con ersely he had great fears for the future of hospitals, nd foresaw a day when the best of our young men will o into simpler and more satisfying institutions—otably general practice

## The Widdicombe File

### XXI MERE?

EAR JAMES

As young James no doubt will have told you by now is job seems to be in the bag There are the usual ormalities to be gone through of course but the old man kes the look of him, and I expect he'll be drawing his icroscope from our store and booking his six feet of ench in a month or so

There's a thing I want to talk to you about like a utch nephew though James Young James tells me—nd indeed it can be read between the lines of your last tter to me—that you're not in the least proud that he's llowing in your footsteps Which is a sad state of fairs, isn't it? But it's a symptom you know James, a disease very widespread among pathologists—an cessive modesty about our own science How many mes have I not heard you get up at some society eeting and begin in tones of abject apology Mr airman if a mere morbid anatomist might venture Mere *morbid anatomist! What you had to say* is always good sense often much needed good sense, d often as forward looking as any of the speculations minor sciences but it was in your view mere morbid atomy to be heeded but not honoured There are a w of the old generation of pathologists who believe in eir subject and a few of mine who think they've discovered it but most of those who fruited between o wars wear a blighted air of eternally apologising for e smell of formalin

There are two main reasons for this one historical but hemeral the other psychological and perhaps inescap le Historically we live still in the shadow of the down that followed the excessive pretensions of the rman school For well over a century, beginning with orgagni plain honest morbid anatomy was the master science of medicine We need go no further than the classic works of Addison Bright and Paget to admit that (Lord knows what *one would call the master science* nowadays the bacteriologists captured the fiery cross fairly from us somewhere about 1880 and the applied physiologists I suppose came next but which of a score of contending disciplines one should recommend to the aspirant for fame I don't know which I suppose is a healthy sign ) But not least of the diseases of western civilisation for which we can blame Mittel Europa is the exploitation of morbid anatomy Virchow was a very great man second to none of our champions except Pasteur and perhaps Lister in their century And Rokitansky and Cohnheim and Waldeyer and others were also mighty men in their generation But they and their followers built up a fantastic machine which went on under its own steam long after its original inspiration had run down Leaving Virchow himself on one side, the German Austrian school made at the time rather less than their fair share of discoveries in pathology but they wrote ten times as much about it Who hasn't struggled with those terrible German articles of yesteryear (did Ewing really read all the references in his *Neoplastic Diseases* I wonder?)—fifty pages of unsignposted text with two useless illustrations, ten of the pages devoted to cell by cell description and the rest to polemics all based on perhaps one new fact that it's a day's work to locate Even today *Virchow's Archiv* but that's another story What wouldn't Matthew do to that so expensive journal!

By about 1890 the view that all good pathology was German was thoroughly fashionable and for the next forty years all good pathologists went to Germany or Vienna to sit at the feet of one Herr Professor or the other I have a vision of you James in your impressionable youth, standing among a cosmopolitan crowd of devotees ranged in two lines down the hall of Aschoff's Institut at Freiburg while the Chief marched between the rows waving a bloody heart beneath your noses and drove *into your avid minds an unalterable dogma* There was a long period when nine tenths of the pathology in this country was secondhand German pathology It's not surprising that in time the non pathologists reacted rather violently Morbid anatomy isn't all of medicine, morbid anatomy for its own sake is only quite a small part of medicine When the Bayliss Mellanby Lewis school of physiological medicine attacked (the Eumenides come to punish our *hubris*) we crumpled badly Much of their more virulent darts were mere Sir Tommy rot but still we crumpled and to be a 'mere morbid anatomist' has been a term of derision ever since

That's mere temporary insanity: we are already past bottom dead centre and on the way up again But there is one disability under which pathologists labour and always will We are all shy men Granted many of us overcompensate and behave with excessive heartiness or are even aggressively rude it is still true that at bottom we are shy Let me expound The satisfaction derived from the practice of medicine by its best practitioners resides chiefly in the employment of a highly personal intellectual skill for the immediate uncomplicated benefit of their fellow men It is possible to feel to the full this generous fervour and yet to find that faced with the individual patient one loves him less than one should and this is often due not to misanthropy, but to a simple failure of the capacity more born than made for the establishment of that instant rapport with other men which is so essential to the successful clinician I do not think we should be ashamed of admitting that in this sense most pathologists are clinicians *manques* In one way or another from those who have frothed up into the cloud-cuckoo land of psychiatry to those who have withdrawn into the surgery of one organ from pure researchers and statisticians to editors and members of

Parliament, many of the brightest ornaments of our profession are refugees from the clinical front line But the isolation of the laboratory tends to exaggerate the primary defect, and pathologists do on the whole seem even to themselves to be a rather ungracious lot compared to many of our colleagues But the fault, dear Jacobus, lies not in our science but in ourselves, that we are unglamorous Let us not therefore repine, and grovel, and look hangdog Glamour of a sort is necessary to the clinician to the pathologist (unless indeed he teaches undergraduates, when it will help him for the first week or two of term till they find him out) glamour is as incongruous and unnecessary as an orchid buttonhole on a coal-heaver

There's something to be said for every branch of the work we do Even post mortems It's a mucky job, and hard work, and few normal people I think really relish its actual doing—and fewer still find it easy to confess to their fiancées or their children just how they earn that part of their living But post mortems can be infinitely exciting real life is always better than the best detective novel

> " World is suddener than we fancy it
> *World is crazier and more of it than we think*
> Incorrigibly plural "

—there are few better illustrations of Macneice's dictum than that ever-surprising four dimensional puzzle presented by the body at the end of a lifetime of varied assaults and defences and few satisfactions greater than that of making the pieces fit And the job is vital enough the P M room is almost the only independent conscience left to a hospital nowadays A hospital whose consultants never see a post mortem has a rottenness at its core and it is often the pathologist's fault if they don't (What a knife edge must we often walk between the carping Charybdis of the cheap jeer at a wrong clinical diagnosis, and the soothing Scylla of the " my colleague, right or wrong " attitude—but how worth while it is to find it )

Important though post mortems are, the whole orientation of most pathological departments has been altered in the last twenty years by the steady rise of biopsy work Histopathology used to be chiefly the art of telling the surgeon what kind of lump he had taken out—an esoteric affair of limited practical importance, with few skilled practitioners The tremendous increase in the use of the biopsy as a means of diagnosis—by physicians even more than surgeons—has profoundly altered this We have far more work, and what there is is a great deal more interesting and valuable Our relation to our hospital is becoming curiously similar to the radiologist's. He sees more patients, and sees them sometimes in motion we see a little deeper, and on the whole our diagnoses are more reliable but we get more and more like each other, and what might be called our public relations and administrative problems are very much his What a game histopathology is !—one of the most difficult arts of medicine, wearisome without end to learn, exasperating to the end, yet ever and again with its rewards of sudden illumination

That's all very well, you may say, James , the routine's valuable and very much more interesting than it looks but how about research ? Nowadays you can't hit the headlines without estimating the lacrimal excretion of radio ytterbium-labelled preposterol, or inventing a five dimensional tensor vector E E G , or growing the virus of onychogryphosis in crocodile's eggs How can I convince people that research in straight pathology is worth while ? Simply enough The answer is just as Vesalius had to come before Harvey, morphological research has always to precede physiological but the second stage of this process is always the more spectacular of the two—simply because it scoops the pool provided by its predecessor There's a singul apt parable provided by the reputations of those two g American cardiologists, Maude Abbott and Helen Tau Maude Abbott worked forty years on congenital hear and produced an Atlas which everyone has heard though few read Helen Taussig sorted out what t anomalies Maude Abbott had described meant in term function, and she and Blalock scooped a sensational p It was wonderful work don't imagine for a mom abate anything in admiration of it, but don't take M Abbott for granted Without the anatomical ground it couldn't have been done

If the surgery of congenital hearts had never b invented, Maude Abbott's Atlas would hardly have b heard of outside her specialised field The same app to all exploratory, observational, recording resear One can never know what part of the field is going to illuminated suddenly by the searchlight of pract application An observational research is never who done No barber shaves so close but another finds wo and moreover observations are like translations from t Greek, and need to be done afresh for every generati Whoever believes that there is no more worth w research to be done in morbid anatomy is either a f or blind We make discoveries slowly, but they st This business of Barr's about sexing nuclei—what object-lesson it is in the way things can stare us in t face for years without ever being seen ! How many ot things must we be looking at every day without seei them ? Morbid anatomy was dead, they said, in t early '30s but the Kimmelstiel Wilson kidney and t *diabetic retina, the pathology of crush kidney,* vir hepatitis, retrolental fibroplasia, and molluscum sebaceu are all stories which have broken since then, and in th list I have included only a few common important th We progress, slowly perhaps, but genuinely and i cease to progress the whole edifice of physiolog research will go on without noticing it much for te twenty years, and then lose itself in a maze of the that have lost that feet on the earth check which supply better than anyone else can

We accept too easily the idea that observati *research and the experimental method are two* diffe things (I see it is fashionable nowadays to ascribe t invention of the experimental method to Grosset Bishop of Lincoln perhaps I shall protest less w next Peter junior calls me " big-head ") An experim is not something you do with spectrometers or guinea or Geiger counters if you are merely amassing d you may use ten isotopes and a thousand mice with doing, truly, an experiment If you make a hypot based on evidence, and then set about collecting n data to test that hypothesis and abide honestly by result, you are *acting* in the best experimental tradi even if your new data are acquired by mere inspectio organs or microscopical slides or even the library I the attitude of mind, not the technique, that matter

Which is not to decry technically experime research (Our mice have got ectromelia again, tho which would give me an excuse for any amount decrying ) But that is open to all men, even thou may still call itself pathology I am speaking only o kind of research that is inherent in the activities of who call themselves pathologists on hospital staffs *I think it's good and necessary*

I've lectured you long enough Don't let me puff up with false pride, James Stay humble, but be hu rather before the infinite complexity of man's body before the pretensions of other disciplines Let model be Jeanie Deans rather than Uriah Heep will do our best to keep young James proud of be pathologist

Yours,
PETER DA

# In England Now

*Running Commentary by Peripatetic Correspondents*

MOST doctors wisely refrain from giving medical advice n second hand information about symptoms, but I ave lately had two vicarious patients whose progress uggests that advice based on vague information is ometimes worth acting on

The first was a middle aged man who developed mysterious alling attacks with loss of consciousness. These caused grave oncern many serious possibilities were discussed and phenoarbitone was prescribed A letter from his wife read out t my breakfast table gave a perfect description of cough yncope *A recent paper on this subject was therefore sent* o the patient's doctor and no more was heard of these ttacks.

I heard of the second patient when an English doctor sent ne a letter she had received about a relative in America who was becoming mentally disturbed and was being treated or hysteria. A letter written by the patient herself showed mong other evidence unmistakable evidence of dysgraphia wrote to the English doctor suggesting that a left hemisphere erebral tumour was likely and that a good brain surgeon hould be consulted without delay This advice duly crossed he Atlantic and was acted on with remarkable speed despite onsiderable resistance from the patient's advisers. Two and half weeks after the first letter was written a cable was eceived in England Successful removal benign brain tumour size of egg Apparently the patient was critically ill at the time of operation and a malignant tumour seemed likely but at operation a large meningioma was easily removed from the surface of the brain and complete recovery followed

In medical work it is sometimes the simplest acts which are of most consequence while some of our present-day complex procedures too often pay insignificant dividends

* * *

Opinions vary on the usefulness of oral penicillins; and hospital doctors, who can inject penicillin in a few seconds with the aid of nothing more strenuous than a fountain pen see the problem a little differently from heir friends in general practice

Last week I prescribed oral penicillin for a small boy with bronchitis I was horrified to find later in the day that the medicine had proved so much to his liking that he had taken the whole bottle-full at a single dose Appalling thoughts of overdosage *poisoning and stomach* washouts passed through my mind After ordering an ambulance I rang the local hospital to warn them of he impending arrival. The house-physician on hearing hat 12 million units of penicillin had been swallowed y a boy of seven gave it as his opinion that that was no earthly good—I should *inject* a million units straightaway

* * *

I took Justin our young anæsthetist down to the nd of the jetty and we began to prepare our lines. The golden grey mullet were moving darkly in the black green waters below and I hoped for a good catch Everything seemed right—the sea was fairly calm the wind low and southerly the sky flecked with high cloud everything seemed right—that is except Justin who has a natural genius for getting into trouble He seems to live on he brink of chaos and is always more than half inclined to all into the abyss On our last fishing expedition—the Hospital Anglers Outing—he had walked quietly and with infinite dignity off the edge of the weir into the river and emerged many minutes later when the rest of s had abandoned hope more than 100 yards downstream ith his pipe still clenched between his teeth and his ot and rod in his hands To the immense edification f the party he picked his way out of the water attached new fly to his line and walked back along the weir o the exact spot from which he had fallen; he then ast with consummate grace and skill across the tail of e fish run as though nothing had happened There always an impeccable aristocracy about Justin's ehaviour of which no-one is more keenly conscious han himself

Standing on the jetty behind us was a young visitor from London immaculately over-dressed in the mock Edwardian style of the day He smiled indulgently as Justin was trying to restore order to his line Justin scowled I was about to drop my live bait into the sea when a cormorant, attracted by the fish suddenly swept up from the waves and alighted on the railing between Justin and me In a last despairing effort to unravel his line and sinker Justin was swinging it round his head in ever-increasing circles. The line went spiralling round the cormorant's neck and in a moment the bird was captured I was too amazed to speak The Edwardian, deeply impressed had lost his smile Cor blimey!" he gasped, Is that the usual way to catch em?'

Justin who appeared unmoved, looked slowly all the way down his long patrician nose 'And pray,' he said, what method would *you* use?

* * *

Beer may be best at home, but as all the world knows Americans like soft drinks. The reason for their addiction to Coca Cola is obscure Possibly the secret lies in the fact that each bottle contains about $2^1/_2$ grains of caffeine Whatever the reason coke machines are to be found everywhere—in canteens, shops, factories, outpatient departments hospital corridors outside operating theatres, and even in post-offices They are of ingenious design Insert your coin and down comes a refrigerated bottle and your change An opener is handy, and a crate rack for empties stands at the side of the machine. At medical conferences the manufacturers supply the stuff free and in unlimited quantities They deserve their ultimate *dividend for this contribution to the prevention of sleep* and dehydration

* * *

Few doctors can put their hand on their heart and say I have never given myself drugs ' but many can say, with Sir Joseph Porter 'Hardly ever Aspirin once in two years for a headache and an occasional barbiturate *for sleeplessness is my normal indulgence but last week* two nights poor and disturbed sleep had lowered my morale and a day's hard work strengthened my determination to have a really good night. So at 19.30 (I always use the 24 hour clock) immediately before supper I took two capsules from one of my boxes of samples. All was well until I was about to tackle some apple-pie with cream (the Queen of my puddings) when my wife noticing my vacant expression accused me of being drunk I had enough sense to tell her of my misdemeanour After some unjustifiable resistance and supported on both sides I was led to bed muttering as I went that I must send the firm a testimonial I was undressed and fell into bed and a sound sleep disturbed soon after by the visit of my doctor who comforted my family and gave me a good prognosis. He was fully justified for the next day I did my daily round and tasks. By a curious coincidence a friend from abroad came to stay She had not recovered from a severe operation and asked if I could prescribe something for her insomnia With what rapture I presented her with the remnants of my sample

* * *

Enthusiastic junior staff sometimes lack the verbal discretion of their more mature colleagues Our surgical registrar and *his house-surgeon lately had occasion to* write up their separate sections on a form for cremation and it had been agreed that the H.S would collect dues from the undertaker Later he breezed into the casualty room and with no heed to a crowd of attentive patients cried: Cremation form—here's your two guineas With commendable presence of mind the S.R said 'Ah yes thank you—just managed to scrape in third I gather—a good race A financial transaction that might well have caused misgiving among the bystanders was given the verisimilitude of one which no-one present would do other than approve

* * *

I always know what to give a lady said my bus conductor (not to me unfortunately) First I give her a Guinness and then I give her a gin-and-cloves—a lovely drink for a lady—and then I give her a good strong port"

# Letters to the Editor

## USE AND ABUSE OF ANTIBIOTICS

SIR,—I fear your correspondents of Dec 18, Mr Grainger and Mr Elliott, have been misled by the necessarily brief account which you gave of my remarks at the conclusion of the joint meeting of the sections of general practice and medicine at the Royal Society of Medicine You report that I had been " struck by the fact that 50% of the drug bill of every large hospital was for penicillin " We were discussing antibiotics, and I was referring not to the total cost of drugs, but to the expenditure on antibiotics, and stressing that despite the criticisms which had been levelled against penicillin, it remained the most widely used of these drugs On the last available figures, every large hospital in my own region (which I had no reason to doubt reflected the general picture) was spending approximately 50% of its total antibiotic costs on penicillin despite its decrease in price, and the advent of newer antibiotics Precise figures for the whole region and for the United Liverpool Hospitals are as follows

*Liverpool Regional Hospital Board*

| *Year* | *Antibiotic cost (% of total drug cost)* | *Penicillin* | *Streptomycin* | *Chloramphenicol* | *Aureomycin* | *Other antibiotics* |
|---|---|---|---|---|---|---|
| 1950–51 | 29 % | 67 % | 33 % | — | — | — |
| 1951–52 | 40 % | 51 % | 49 % | — | — | — |
| 1952–53 | 40 % | 48 % | 30 % | 13 % | 9 % | — |
| *1953–54 | 36 2 % | 41 % | 29 % | 10 % | 11 % | 9 % |
| *The United Liverpool (Teaching) Hospitals* | | | | | | |
| 1952–53 | 32 9 % | 61 % | 12 % | 18 % | 9 % | 0 3 % |
| *1953–54 | 30 1 % | 57 % | 11 % | 12 % | 12 % | 8 % |

* The returns of 1953–54 have become available since the symposium and show a small fall in the cost of penicillin

My plea for discrimination in the use of especially the newer antibiotics was not based primarily on economy, but on their potential hazards both to the individual and to the community

Liverpool HENRY COHEN

## PSYCHOLOGICAL ASPECTS OF UTERINE DYSFUNCTION

SIR,—In his article of Dec 18 Dr Cramond concludes that " psychiatric methods of prediction and prevention in the antenatal period would have no effect on the occurrence of uterine dysfunction " While this may well be true of the psycho analytical approach it is not a logical deduction from his paper, nor is he entitled to conclude that " fear, emotion, and anxiety play no part in the outcome of labour from the practical obstetrical point of view " Neither his control nor his " dysfunction " group were given any sort of physical or psychological preparation unless we count the eighteen who attended " talks on pregnancy and childbirth " There remains a possibility therefore that uterine function in both groups might have been improved by good preparation and that some of the " dysfunction " group might have avoided their forceps and sections

The fashionable rejection of preparation for childbirth is too often based on slender grounds, the preparation having consisted solely of a few " relaxation " classes and a lecture or two Numerous workers have found a more thorough preparation of value Dick Read, while one can dispute his physiology, undoubtedly influenced the course of labour in his patients

In France workers at the maternity clinic of the Pierre Roques polyclinic, basing their work on Pavlov's theories of central nervous physiology (perhaps Dr Cramond will find these equally obnoxious), are also demonstrating the very real influence of what they call " psycho prophylaxis " on labour Their methods include (*a*) explanation of the facts of pregnancy and labour, (*b*) explanation of the rôle of tradition and false attitudes in lowering the cortical threshold to pain by implanting false conditioned reflexes, (*c*) an attem to replace these false attitudes with healthy ones, (*d*) instructions in methods of muscular relaxation a respiration Finally, great stress is laid on a factor usual neglected in this country—the need for the const presence throughout labour of trained staff to assist t parturient woman in the application of her lessons B these methods some 80% of obstetrically normal moth are delivered without the use of analgesics The aver duration of labour has diminished and the interven rate has dropped sharply in this clinic since the intr duction of these methods[1,2]

Dr Cramond concedes that preparation may allev " mental pain," however this is defined I feel there i evidence that it can do more than this One does n dispute the multiple ætiology of uterine dysfunction claiming that preparation for childbirth can remove, some women, one cause for it In addition preparati can provide for the majority of women having n deliveries an experience always tolerable and enjoyed

London N W 5 ANTHONY RYLE

## HARDENED FATS AND LUNG CANCER

SIR,—Dr Nyrop's suggestion (Dec 18) that th consumption of margarine may be a factor in t causation of lung cancer is based on such slender irrelevant, and sometimes inaccurate arguments that must be challenged

His first point is that the unsaturated essential fatt acids may play a part in protecting the body a carcinogenic agents The only real evidence whic Dr Nyrop quotes for this is the work of Deuel et al,[3] in which rats deficient in these substances were found t succumb rather sooner to carcinogenic doses of X ray *How they react to chemical carcinogens is quite unknow* More important, deficiency of essential fatty acids h never been shown definitely to occur in man

Secondly, Dr Nyrop states that the hydrogenati of fats to produce margarine and shortenings " eliminates essential acids " This is not true Margar contains something like *twice* as much essential fatt acids as butter, and shortenings may contain up to f times as much as butter[4] Rats have been reared f 25 generations (*equivalent in man to some 750 ye* on margarine as the source of dietary fat, and h shown as good health, vitality, growth, longevity, a *fertility as those fed on butter*[5]

Finally, Dr Nyrop falls into the common trap " correlation equals causation " Margarine cons *has increased, so has cancer of the lung, ergo, the f* causes the latter But it is not only the consumpti of margarine which has increased, there has also be *an increase in looking into television and in the* us synthetic fibres for clothing, either of which could equ well be accused of causing bronchial carcinoma T *argument could be used just as reasonably to prove* th *lack* of association between consumption of margar and the incidence of cancer of the lung In countr where there has been little *or no rationing*, the aver consumption of margarine is inversely proportional income, we should therefore expect a similar relati ship between cancer of the lung and economic class fact, the relationship between lung cancer and econo class is slight and its direction differs in men and wom in any event, it does not fit in with Dr Nyrop's br thesis Again, margarine consumption in Holland

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1 Ryle A *Med World Lond* 1954 80 36

2 *Rev nouv Méd* 1954, no 3 (special issue)

3 Deuel H J Chang A L S Kryder, G D Bingemann *Science* 1953, 117 251

4 Deuel H J Greenberg, S M Anisfeld L Melnick *J Nutr* 1951, 45 535

5 Deuel H J Greenberg S M, Savage E F *Ibid*, 1 42 239

ppreciably higher than in Britain but the incidence of ung cancer is approximately half that in Britain

Summarising then, we may say (1) whilst there is ome evidence that deficiency of essential fatty acids enders animals more susceptible to X ray cancer there s no evidence that they are more susceptible to chemical arcinogens, (2) deficiency of essential fatty acids rarely f ever occurs in man (3) hydrogenated fats like mar arine contain more of these acids than the fats such as utter, which they replace in the diet, and (4) the ncidence of cancer of the lung is not generally higher n those groups with higher margarine consumption

Queen Elizabeth College
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JOHN YUDKIN

## OCCASIONAL BRONCHOGRAPHY

SIR,—I was interested to read Dr Glendinning s article in your issue of Dec 18 The method he describes I have used essentially unchanged except as regards the actual local anæsthetic for the past sixteen years or so with complete satisfaction in very many more patients than the occasional case '

Atropine injected a half to one hour before the examination commences is invaluable and I do not hesitate to increase the dose from gr $^{1}/_{100}$ to $^{1}/_{75}$, or even gr $^{1}/_{50}$ in the chronic bronchitic whose mucous membranes are generally much more moist than those of the average person

As a recent refinement I find that a tablet of amethocaine (gr $^{1}/_{2}$) given to suck a few minutes before the spraying begins gets over the gagging ' of the sensitive or nervous patient who resents the approach of a throat spray Incidentally I find 2% plain lignocaine ( Xylo caine ') quite adequate (which increases the safety margin till further) and by using a De Vilbiss syringe can get my spraying direct on to the cords After intubation in the chronic bronchitic I inject 1 ml of the lignocaine solution down the tube a minute or so before following t with the opaque medium

There are a few patients who have the knack of saying e ' quite well with a small catheter between their vocal cords, and I find the simple trick of aspirating air up the catheter confirms the correct lie of the tube If he tube is in the trachea aspiration is of course easy and ompletely devoid of resistance and injection is equally ffortless with the tube in the œsophagus aspiration of air s either impossible or intermittently possible against a eeling of resistance

The virtue of the method Dr Glendinning has described s that in the hands of the tyro the worst that can happen s a failure of the examination, and with reasonable care satisfactory examination is carried out with little listress to the patient In the hands of the expert it ives an opportunity for detailed filling of any area or reas without hurry and, if necessary under screen ontrol

Central Middlesex Hospital
London, N W 10

F PYGOTT

SIR,—Dr Glendinning provides a valuable description of a very pretty bronchographic method and suggests hat patients would much prefer tracheal intubation to ricothyroid puncture I have used a similar method of ransnasal blind intubation for some years and although agree it is free from the dangers of cricothyroid punc ure, patients who have been subjected to both methods ay without exception they much preferred the crico hyroid route Dr Glendinning does not mention the lifficulty I have sometimes found in passing the tube hrough the conscious patient s nose and in making it url down into the pharynx Questioning patients and ractice on myself suggests that this is the most uncom ortable part of the procedure

King's College Hospital,
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FRANK RACKOW

## A FILM ON MENTAL NURSING

SIR,—I read in your issue of Dec 18 the report of the film *The Troubled Mind*, and looked forward to seeing it on the television programme that night Having seen it I find my mind very troubled

The object in producing this film was to show it to the general public in order to attract recruits to mental nursing Surely sight must have been lost of the effect this film will have not only on the parents of recruits, but also on patients who may require treatment in mental hospitals and their relatives

For many years now a great deal of time has been spent and much work has been done in enlightening the general public on mental illness, and encouraging the mentally ill to come voluntarily into hospital for treatment That this effort has been justified is shown by the fact that between 70% and 80% of patients now come in voluntarily some hospitals claiming an even higher percentage of voluntary admissions

The general public the relatives of the mentally ill and the sick patients themselves nearly always conceive the mental hospital as being populated by patients obviously deranged obviously disturbed and obviously requiring segregation The fear of entering a mental hospital is so often based on this conception that admission is refused on the grounds that the illness is not bad enough or will become worse as a result of mixing with such patients.

This film in my opinion serves only to confirm these misconceptions, and I now fear the results It is obvious that patients could not be used in the film but the rôles played by the members of the staff of Shenley to depict patients were poorly portrayed and grossly over acted If patients themselves could have been filmed I am sure that they would have appeared more normal and that even the scene showing the disturbed ward would not have included (in any one day) all the deranged behaviour shown In the incident of the male patient refusing occupational therapy was it necessary to indulge in facial twitching in order to be recognised as a patient ?

Hysterical attempts at suicide impulsive smashing of windows furious digging in the gardens deliberate destruction of shrubs were all shown as the common everyday behaviour all manifest at practically the same time and even those patients walking in the grounds of the hospital were openly mental ' Except for the scene of the small group in the room saying they had come voluntarily on whom only a few moments were spent, there was no suggestion of the normality of which as you rightly point out, newcomers to mental hospitals remark But these are normal people.

Why must electroconvulsion therapy be shown as distressing to the new nurse when modern treatment using muscle relaxants routinely produces practically no visible signs of convulsion ? Why must occupational therapy be represented by cane work ? In a fairly recent comedy film the hero is shown doing cane work to infer his admission to a mental-observation ward much to the amusement of the audience

More student mental nurses are very sorely needed They are required to be trained to nurse the mentally ill and to help in the treatment of the acute cases and in the nursing and rehabilitation of the many long stay patients who for lack of sufficient staff tend to be withdrawn idle slovenly and incontinent Nurses are required in larger numbers so that each can have a small group of patients for stimulating interests for encouraging habit training for occupational and recreational therapy for nursing the physically ill and for encouraging the aged to be ambulant The concern for patients must continue to be fostered and not as in the film trained into apparent indifference as shown by the ward sister towards the suicide attempt

I doubt very much the value of this film in recruitment The film is courageous but it does not show the training and work of a mental nurse in true perspective It does harm in placing before the public a picture of mental hospitals which is not in accord with conditions today I fear it may only indirectly help to solve the problem of the shortage of nurses in mental hospitals—that is, by discouraging from voluntary admission a large number of patients in need of treatment

Bexley Hospital
Kent
M RADZAN

## A WORD WANTED

SIR,—May I, with some diffidence, point out that, in his letter in your issue of Dec 18, Dr Todd is in error The meaning he ascribes to πρός is in fact that of πρό and it is from this word that πρωί is derived

There already exists an excellent Greek word, πρόσκοπος ("seeing beforehand"), the English form of which would be "proscopic" Since the true superlative of πρό is πρῶτος (first), an alternative and more emphatic adjective would be 'protoscopic'

DOCTOR'S HUSBAND

## PATIENTS' DAMAGES

SIR,—Most of your readers will agree that the great majority of cases of medical negligence in which no special clinical or pathological knowledge is required can be effectively and fairly dealt with under the present system It is in the vitally important minority of cases where such knowledge is essential that the courts are placed in the invidious and impossible position of having to assess clinical judgment in retrospect The remarkable change in legal interpretation as a result of the 1946 Act seems to result in pronouncements which, as I pointed out in my original letter (Oct 30), often seem to be inspired by the view that this *legislation guarantees* the patient not only treatment but cure

I was at no time enamoured of the idea of taking medicine outside the law my concern was wholly—and not at all incidentally—with the ethical sequelæ of this change in judicial interpretation, and it was solely for the safeguarding of these principles that medical representation was advocated in the *investigation* of such negligence Legal convenience was not my concern, but a leading article in the *Times* of Dec 18, while not concerned with professional freedom, does suggest an arrangement by which both medical and legal interests might properly be served

> "Administrative tribunals, whose decisions are enforceable as law, have no doubt come to stay They do, as a rule, dispense fair judgments—comparatively cheaply—over a great range of subjects on which the Queen's judges have, and would claim, little competence to pronounce The need for them arises from the overruling by legislation of private rights, generally property rights but sometimes rights of personal liberty, for the sake of public advantage"

It is ironical to note that the letter instigating this exposition was concerned not with advocating the establishment of such tribunals, but that there should be easier appeals from their decisions Medicine is thus not one but two steps in arrears!

This brings the argument full cycle The problem remains, but it is only fogged to those of us who are good administrators or indifferent doctors The evolutions of both medicine and the common law possibly through regard for each others' special function, have traditionally been in parallel, and the results have dovetailed for the welfare and well being of the community But now they are to some extent in collision, and there may be many of your readers who are concerned that the standard medical contribution to medicolegal controversy seems too often to be that of gratuitous apology which, rightly or wrongly, presents the picture of a profession in flight from its principles, and content to accept t clinical intuition of Her Majesty's judiciary

Royal South Hants Hospital,
Southampton
P FARM

## TUBERCULOSIS IN IMMIGRANTS

SIR,—I should like to endorse most strongly the opin of Dr Sevitt (Dec 18) that the solution to the prob of how to protect the health of the Irish immigrant in close and friendly cooperation between the British Irish health authorities *Attempts at compulsion* unnecessary and probably inapplicable, moreover, are likely to arouse strong resentment and so befog t real issues I can see no clash of interest whatev between the Irish and ourselves over this matter, it in their interest that their subjects over here rema well and in ours to keep them well Let us thrash our mutual difficulties amicably, sensibly—and togeth

Clare Hall Hospital,
Barnet
NORMAN MACDONALD

## TRYPSIN INHALATION IN BRONCHITIS

SIR,—I was very interested to read the letter fro Dr Oswald and his colleagues in your issue of Dec 4

I do not think that trypsin has a place in the treatme of the ambulant chronic bronchitic, but, if effective, i would have a very definite place in the treatment the acutely ill emphysematous patient who is unable t raise sputum because of its tenacity It would also help in the management of the emphysematous patient who having got over his acute respiratory infection, becom chronically anoxic simply because he cannot get rid o the tenacious sputum Chronic anoxia results in mor and more lethargy and inability to concentrate and he less desire to cough In fact the mental state may such that the patient is thought to be just "pl awkward"

Exsufflation with negative pressure[1] is used in th U S.A in the treatment of these patients, as is inte mittent positive pressure breathing,[2] which also help to get the aerosol deeply into the lungs. Both metho require the cooperation of the patient, and they costly and, so far as I know, unavailable in this countr

I have used 'Trypure' in a patient aged 57 who w admitted on Oct 14 in semicoma due to an acute respirator infection complicating a severe degree of emphysema. H wife said that he always had difficulty in raising sputum O admission arterial blood analysis showed a pH of 7 25, a pCO of 69 mm, and an oxygen saturation of 49% One m later the oxygen saturation had risen to 71%, the pH 7 33, and the $pCO_2$ 56 3 mm At this point, although cyanos he was mentally clear

Since then his cyanosis has increased, owing, I think, to inability to get rid of the sputum, and his mental state h deteriorated Arterial blood analysis now shows a pH o 7 30, a $pCO_2$ of 62 5 mm, and an oxygen saturation of 45% Although the $pCO_2$ in repeated blood analyses has shown tendency to rise slightly the oxygen saturation has remain almost constant He will not tolerate oxygen therapy Trypu has been used, therefore, to loosen his sputum It has be given through a Collison inhaler using 8 3 mg in 2 5 ml o the buffer on the first, double the amount of both on th second, and three times the amount on the third day Th dosage was used in order to avoid waste since trypure i supplied in 50 mg phials with 15 ml of diluent and wh mixed must be used at once On the following day I divid the 50 mg into three equal parts and gave three inhalatio at 4 hourly intervals

Although there was no immediate improvement in h general condition he has raised more sputum on these s subsequent days, and 5 days later his mental condition becam quite clear and the arterial blood showed a pH of 7 29 $pCO_2$ of 60 mm., and an oxygen saturation of 60% Whethe this improvement will be maintained or not I do not know but all the evidence suggests that it is due to the action o

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1 Barach A L Beck G J *Arch intern Med* 1954 93 8 Beck G J Barach A L Smith W H *Mod Hosp* Janua 1954

2 Motley H L *Bull N Y Acad Med* 1950 26, 479

ypure in loosening the sputum If I had had the complete operation of this patient or a more effective method of tting the trypure into the depths of the lungs a better result ight have been obtained

I would suggest that an assessment of the value of ypure be made not on the ambulant bronchitic whose utum varies in character and amount from day to y but on those who are either acutely ill or chronically oxic because of the inability to get rid of tenacious utum

My thanks are due to Evans Medical Supplies Ltd for the pply of Trypure

Chase Farm Hospital
Enfield Middlesex
THOMAS SIMPSON

## ONG TERM CHEMOTHERAPY OF TUBERCULOSIS

SIR,—We were interested in Dr Mitchell s comments Nov 13) on our article of Oct 2 We hope to publish hortly the results of one year s treatment in the two roups of patients whom we have investigated and there o deal in greater detail with the important problem of revious chemotherapy

C L JOINER
J D CARROLL
ROBERT KNOX
K S MACLEAN

Guy s Hospital
London S E 1

## CONTINUOUS INTRAVENOUS OXYTOCIN

SIR —The article by Mr Holmes in your issue of Dec 11 is of great interest to those attending women in abour

At the obstetric clinic of the University of Geneva[1] imilar experiments were carried out in 1949 on 91 cases nd the conclusions reached were comparable to those f Mr Holmes It was felt however that a 5% glucose olution was to be preferred to physiological saline or the following reasons

(*a*) The heavy demand made upon the uterine muscle uring labour especially after oxytocin administration equires an increased intake of glucose An intravenous drip s indicated especially in cases where feeding by mouth is eing withheld in view of possible anæsthetics

(*b*) Oxytocin increases liver glycogenolysis. The hepatic lycogen reserve may be considerably lowered and it is herefore advisable to replace the loss by additional intake of lucose

n no case was venous thrombosis observed

The Marie Curie Hospital
London N W 3
RACHEL WERBLOWSKY

## RASH ON THE SOFT PALATE

SIR —I was struck by an illustration in Dr Holzel s rticle of Nov 20 of a soft palate rash and I said at nce Alexander s sign In early 1919 there appeared n the bulletin of current medical literature issued to the R.A M C a précis of an article by a Russian physician Alexander who described a soft palate rash as a diag nostic sign of true influenza This rash he affirmed to be on the soft palate and to be punctate and erythematous with some œdema which outlined the junction with the hard palate It was unlike that noted in infective mono nucleosis in being rarely petechial

As we were in the middle of an outbreak of true nfluenza at that time I was soon able to convince myself that the rash always did occur in the first few lays of true influenza and that it did not occur in he common forms of febrile rhinitis &c which are commonly called influenza

Since that time I have found that this rash is of great help in the differential diagnosis of true virus influenza But I have never heard of any other physician who vas acquainted with it

Bitton near Bristol
A T TODD

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1 Werblowsky R. University of Geneva thesis no 1963 1950

## MASS TUBERCULIN TESTING

SIR,—In your otherwise admirable leader of Dec 18 I was alarmed to see the re birth of an old idea that mass miniature radiography units should be diverted to mass tuberculin testing—a course which can only lead to a reduction in the total output of these valuable units at a time when more and not less chest radiography needs to be done. Probably less than 30% of our adult population have ever had an X ray examination of their chests and one of the problems before mass radiography is to include in its scope those not previously X rayed Ideally this would be the whole of the remaining 70% but with the limited resources available it is to be expected that only selected groups can be surveyed In my view this can now be achieved only by an intensive and nation wide propaganda campaign on a scale at least as powerful as that devoted to diphtheria immunisation or the sale of detergents It is a practical fact that the limits of local propaganda have been reached

The essential element of mass radiography which distinguishes it from other forms of chest radiography is the speed at which the film passes the shutter of the camera Nothing must be allowed to slow this speed Although the staff of the present units have considerable experience in approaching the public and in the organisation of mass campaigns, their function is in no other way connected with tuberculin testing and the two should not be confused Thus though there might be some virtue in a loose association between a tuberculin testing team and a M M R. unit in order to pool certain resources and experience any attempt to fuse the two would be to the advantage of neither and the detriment of both

The level of tuberculin positivity is still high enough in the adult population to merit mass X ray examination without previous tuberculin testing and although it is often claimed that the discovery of a positive tuberculin reactor leads to the discovery of a source case it is equally often forgotten that the discovery of a case by M M R. also leads to another one by proper surveillance of contacts Mass radiography has a vast task still to do ; let it not be diverted to other pursuits till that task is finished

One further point If mass tuberculin testing is to be done, then the sooner the better and before the scene becomes shrouded in the mists of tuberculin positivity created by B C G

London W 1
F D BEDDARD

SIR —In your leading article Mass Tuberculin Testing you say that the proportion of London school children positive to tuberculin is startlingly low

I would have thought that this would have been an expected finding in view of the efforts made both nationally and locally against tuberculosis. What is most significant is the figure you give of 75% of the 6 5% positive reactors in the mid Wales survey which were traced to a human source This draws attention to the inestimable value of the tuberculin test as a weapon in the hands of the epidemiologist in the tracing of spreading infection

In the past when the number of positive reactors in the population was high the use of the tuberculin test was very much limited in this field ; but now that there is such a high proportion of negative reactors we must be careful to make capital of this position in the control of tuberculosis Mass B C G immunisation will destroy this present advantage and until we have more valid statistical evidence of the value of B C G we would do well to hasten slowly

Manchester 3
IAN G TAYLOR

SIR —I was interested in the article by Dr Carroll Palmer and his colleagues and by the leading article in your issue of Dec 18

Unless the reasons are very strong, I think it would be a great pity to replace the 10 T U intradermal tuberculin test by one of 5 T U In this country, largely as a result of the Prophit Survey and the recommendation of the Ministry of Health (memo 324/B C G ), the 10 T U Mantoux test has been in general use as a screen test and many of us are now beginning to feel some confidence in its interpretation

I am in full agreement with your leader and with the W H O Expert Committee on Tuberculosis, who insist " that B C G vaccination campaigns should be centrally organised and made part of the general public health programme " , but I am sure the suggested method of carrying out this work—namely, the employment of one mass radiography unit in each region—is not practicable Consider, for a moment, a single group of the community—children in their 14th year The X ray examination and B C G vaccination of these children must be carried out at school during the spring or autumn terms, the summer term being fully occupied with examinations, sports, and other activities

Mass radiography of this group in Cornwall (approximately 4000 children, scattered among 175 schools) occupies the mass radiography unit for nine weeks The population of Cornwall (341,463) is approximately a tenth of the population of the South-Western Region, which includes Devon, Cornwall, Somerset, Wiltshire, Gloucestershire, and parts of Dorset It would, therefore, be quite impossible for one mass radiography unit to carry out mass radiography, Mantoux testing, and B C G vaccination of this single group of the community in the time available Moreover, the mass radiography unit is a highly skilled and specialised unit, adapted for its purpose It would be uneconomic to employ it in routine tuberculin testing and B C G vaccination

For the past two years, Cornish school children in their 14th year, whose parents are willing (approximately 85% consent), have been passed through the mass radiography unit, tuberculin tested, and given B C G vaccination where indicated

The mass-radiography unit visits 11 centres at which the children from the surrounding schools are assembled Tuberculin testing is carried out by the assistant county medical officer or the school medical officer, assisted by the school nurse, as part of their routine duties Three days later, a chest physician visits the school to carry out B C G vaccination An exception is made in smaller, isolated schools, where all the work is done by the assistant county medical officer or the school medical officer The sharing of this preventive work by the director of the mass radiography service, the chest physician, and the local authority medical officer is, I think, of great value in integrating the two sides of the tuberculosis service It has the added economic advantage of not requiring any additional staff

County Hall,
Truro

E R HARGREAVES

## PEPTIC ULCERATION IN SOUTHERN NIGERIA

SIR,—Mr Konstam's observations (Nov 20) on the incidence of duodenal ulcer in Southern Nigeria and the influence of diet open a wide field of interesting and useful research , but I do not think he should so lightly discount the psychosomatic side, because the outward appearance of dignified calm and placidity of the average Yoruba, be he peasant or townsman, is deceptive Having once worked as medical officer in charge of Adeoyo Hospital I found the Yoruba to be highly strung and sensitive, and surrounded by complexities of tribal, family, and personal life which would give the average European an easily explained ulcer The " simple peasant " in the South does not exist He is just as worried about his cassava crop as Mr Jones is over his overdraft The market woman at the hospital gate with a [illegible] pile of groundnuts for sale in front of her is very likely the owner of a fleet of produce lorries and four-figure deals with the Cocoa Marketing Board.

The examination of physiological fluids is child's compared with understanding the intricacies of psychosomatic side of the African

Cape Town

H WATSON SMI

## A BLOOD-TRANSFUSION PUMP

SIR,—A rotary pump for use with all forms of venous therapy was fully described by Mr Victor R in his book, *Blood Transfusion,* published in 1939 was described and illustrated again in Mr Keynes's recent symposium on the same subject

This type of pump provides a simple and effic method for the rapid replacement of blood when th indicated

London, S W 1

ERNEST LANDA

## GOITROGENIC HAZARD OF COBALT

SIR,—We have read with interest the letter fr Dr Gairdner and his colleagues in your issue of Dec 1 We fully agree that cobalt should not be added to preparations for general use, but we feel that it would unfortunate if clinicians were discouraged from pre- ing a drug useful in the prevention and treatment of anæmia of prematurity and other iron-resistant anæm

We have reported [1] the use of cobalt sulphate in premature infants (maximum dose 20 mg daily for fo weeks), and a further paper dealing with its use various iron resistant anæmias in childhood is in press

Over 200 other children, both prematures and with infection, have been successfully treated and toxic effects noted in any case The majority of our were treated from three to four weeks, but in some t ment was continued for eight weeks with no adv results

There is now a considerable literature referring the hæmopoietic action of cobalt in both man animals with no reference to goitrogenic activity the paper quoted by Dr Gairdner, and we feel that beneficial effects of cobalt fully justify its contin use in selected cases under careful supervision

London W 1

URSULA JAMES
B L COLES

## PROLONGED PREGNANCY

SIR,—In your issue of Dec 11 Mr Stenhouse has ask two questions and I should like to reply

When I saw my patient for the first time at 38 wee the presenting part was not engaged and the long firmly closed primiparous cervix suggested that conditi were most unfavourable for an attempt at induction labour I was anxious to avoid anything but spontane delivery, it seemed certain that the position improve with delay for a week or two, and the norm onset of labour was awaited with confidence Q naturally I did not anticipate the actual sequel L when labour was in progress, it became clear that deliv was obstructed With the lowest part of the ceph pole scarcely advanced to the level of the mid pel and with the certainty of seriously abnormal struct still at or above the pelvic brim, embryotomy was in my view a procedure to consider As events prov it would have been extremely difficult and theref dangerous

I have lately found a reference to an analysis of an cephaly by Mr Percy Malpas as long ago as 1933 [2] Th was postmaturity in 9 cases out of a series of 44, and one instance the pregnancy lasted for 374 days

Woking Maternity Hospital,
Surrey

L G HIGGIN

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[1] Coles B L James U *Arch Dis Child* 1954, 29 85

[2] *J Obstet Gynæc , Brit Emp* 1951, 58, 103

## INNOCUOUS TEMPORARY IMMOBILITY

SIR —The condition which was described under the lo Night Nurses s Paralysis in your last issue can cause ich alarm when temporary immobility occurs for the st time and the sufferer is unaware of its harmlessness I have drawn attention in the past [1–3] to the occurrence this condition in persons engaged in other occupations more especially printers Since immobility can occur ring the day as well as the night and in persons other an nurses, the name is clearly a misnomer though it s been in use for many years, and it was used in lectures en to nurses at some mental hospitals in the earlier rt of this century

The condition is widespread and occurs in all climates have known it on board ship in the Arctic Ocean and places as far apart as Montreal Macclesfield Gibraltar d India

In a recent investigation which I conducted 60 male d female nurses were questioned and 25 (42%) knew the condition, 19 (32%) having suffered from one or ore attacks In a previous inquiry [1] of 67 male and male nurses 27 (40%) were aware of its existence but ly 12 (18%) had suffered from attacks The latest vestigation did not add to the 16 conditions from hich the immobility must be distinguished [2] but it led a fuller appreciation of the existence of partial attacks, attacks in those other than nurses and of the further ngers to the subject during the course of an attack

*Partial Attacks* —In 3 cases the ocular muscles were e only ones involved

A matron reported that from time to time when reading the day or night she was unable to move her eyes from e end of one line of print to the beginning of the next. This s so frequent that she thought it was a normal occurrence everyone A female nurse said that her eyes became fixed any part of a line of print when reading at night and a le nurse who also suffered from generalised immobility up to 5 minutes duration timed by the clock, stated that at ght his eyes became fixed for about 30 seconds or so at y part of the line

An observer said that on 3 occasions, he saw a male nurse and stop writing for a few seconds. Suddenly the nurse und he could write again During the attacks the nurse s able to talk and make other movements. One person s able to smile in an attack and 2 were able to talk although distinctly in one case

An observer noted that the male nurse whom he was ho ing was apparently watching him and turned his head wards him but was unable to move until the observer took ld of his arm when he suddenly jumped up

*Attacks in Non nurses* —There were 2 additional finite attacks and 1 doubtful attack in this investiga on

A warrant officer who was sniping in front of his trench in acedonia as he had done many times previously found that though his finger was on the trigger and 3 Germans in his ght he could not fire nor did he answer the telephone beside m until it had buzzed three times. He was asked why he had t fired He then did so

A sergeant was sitting leaning back against a tree in France 7 A M when an officer approached The officer said Get , Sergeant get up but he was unable to move although front of his men The officer had left before he was able to e but the sergeant apologised to him later

The doubtful attack involved a radar operator on a ship o although he saw an object on his screen was unable to port its presence to the bridge The officer on the bridge w the ship and asked him why he had not reported This s not been classified as a definite attack because no other rson was in the radar cabinet and the operator might have en sleeping

*Occurrences During Attack* —A night nurse in a mental spital said he was sitting down when he saw a patient approach him with a chair The patient struck him with the chair and the nurse was unable to defend himself The nurse watched the patient approach so the possibility of immobility due to fear cannot be excluded, although in mental hospitals the nursing staff are accustomed to dealing with troublesome and dangerous patients

This identification of partial attacks raises the question of cause Previously an attack comprising immobility of the legs alone was the only partial attack recorded This further inquiry shows that small portions of the motor system can be affected The site of the failure is obscure, but in view of the observation that small jerky movements may occur before full movement returns it seems that some impulses can get through to the muscles from consciousness As in many cases only one attack has occurred over 30 40 or more years, the condition does not appear to be a permanent psychological condition, such as hysteria This immobility may be due to defective transmission at the myoneural junctions although it is hard to see why only certain junctions should be affected in some cases or why in one man all voluntary muscles were affected on some occasions and only the ocular muscles on others But myoneural block seems to be the most likely explanation particularly since the condition usually occurs when the subject is stationary

Bristol G DE M RUDOLF

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1 Rudolf G de M *Brist med-chir J* 1946 63 132
 Rudolf G de M *J ment Sci* 1946 92 814
3 Rudolf G de M *Ibid* 1947 93 360

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## INTRAMUSCULAR IRON

SIR,—Dr Jennison and Dr Ellis in their article of Dec 18 conclude that local reactions to iron-dextran are seldom important and general reactions very mild We have had two severe reactions recently

The first wa in a man of 54 with ulcerative colitis and anæmia, who was given three 2 ml intramuscular injections of the iron dextran solution on alternate days After the second he complained of local soreness and after the third he had pain in both buttocks and fever to 102 F Over the next forty-eight hours, the outer parts of the buttocks became painfully swollen, red tender and indurated and the inguinal glands grossly enlarged and tender No further injections were given and the condition settled down completely within eight days without suppuration or the use of antibiotics. There was a past history of skin allergy which suggested an allergic basis for this reaction.

The second case concerned a boy of 17 with steatorrhœa and anæmia. He received 1 5 ml of the iron dextran solution intravenously At once he became flushed distressed and restless; bradycardia was noted, and a few minutes later he complained of severe pain in the loins which gradually settled in $1^1/_2$ hours.

It seems therefore, that this iron dextran preparation should be given further extensive trial before its general use is advocated

The London Hospital E 1 IAN P ROSS

## SMALL-BOWEL DISTURBANCES AFTER ABDOMINAL OPERATIONS

SIR,—Your report of Dec 18 mentions a statement by me at a meeting of the surgical section of the Royal Society of Medicine when I gave the figure of 8% for the prevalence of atrophic gastritis after partial gastrectomy My comment was an unprepared reply to the unexpected compliment of a question by the president and I would be glad to extend it

In the past eight years I have gastroscoped an ave
of just under 225 patients a year and the prop
these examined for post gastrectomy symptoms h
fairly steadily (excluding one year when th
333 patients when we made special exam
a week of hæmatemesis) from 0 7°
1954 Of the last 53 gastrectom
atrophic gastriti It would have b
this proportion as a percentage
negligible Professor Witt

earlier in the same meeting 2 of my patients had severe hypochromic anæmia (atrophy confirmed in 1 by biopsy), and a minor group of post-gastrectomy syndrome may be attributed to gastric mucosal atrophy

May I add an example of operative disturbance of small-intestinal function I would have quoted if I had had the presence of mind ? About 1908 a girl, aged about six, was severely burned and developed a stenosing duodenal ulcer Sir Henry Souttar found it necessary to do a gastro enterostomy, and she recovered About 1942 I treated her for microcytic anæmia, and about 1946 for œdema and hypoproteinæmia Shortly after discharge she returned with acute obstruction of the small intestine due to a band apparently connected with her previous operation This was divided and she has apparently remained well since It seems as if obstruction disturbed iron absorption first, protein absorption next, and finally the total arterial supply of the bowel

Hove Sussex W A BOURNE

## STRANGE LANGUAGES

SIR,—During the late war the Army Education Corps put out several useful booklets on foreign languages In view of the large number of Maltese, Somalis, Greeks, and Cypriots entering this country, could not the Ministry of Health publish similar pamphlets, obtainable on demand, for doctors near docks, &c ? They could contain colloquial speech and popular medical terms They would be more useful to me than my extra chair for an interpreter—and a " no smoking " sign in nine tongues

Mile End,
London E 1 N D WAYNE

## MECHANISM OF RAYNAUD'S PHENOMENON

SIR,—Lewis established that cooling of the fingers produces vasoconstriction, followed by vasodilatation [1] He maintained [2] that excessive vasoconstriction alone was the cause of Raynaud's phenomenon, but later observations have failed to support this view

Hertzman and Roth,[3] investigating a mild case of this disease, showed that although vasodilatation did not follow vasoconstriction when the patient's finger was placed in water at 15°C, vasodilatation did ensue when the water was colder (8°C) Greenfield and Shepherd [4] showed, moreover, that when healthy persons placed their fingers in water at 0–6°C blood flow in the digital arteries almost ceased (rapid dilatation followed after 5–10 minutes) It has also been found [5] that the vessels *of healthy persons*, and of those with Raynaud's disease, respond equally to adrenaline

Using the calorimetric method of Greenfield and Shepherd,[4] we compared the vascular response to cold in 20 patients suffering from Raynaud's syndrome with the response in a control group of 20 healthy persons Each subject first immersed his hand for 10 minutes in a water bath at 25°C and thereafter held his finger for 15 minutes in a calorimeter at 9 5°C [6]

We observed that

(1) The degree of initial vasoconstriction was the same in the two groups

(2) In the control group dilatation ensued after 4–6 minutes in 18 cases, during the 7th minute in 1 case, and during the 8th minute in another, in the patients with Raynaud s syndrome no dilatation occurred in 13 cases during the 15 minutes, and in the remaining 7 cases it occurred later, and to a lesser degree, than in the controls

This suggests that the essential difference between healthy persons and those with Raynaud's syndrome is in the capacity of their digital circulation to respond to the stimulus of cold by vasodilatation We attribute this to a local vascular defect in the mechanism dilatation

No noxious agent is known which increases the resp of vessels to constrictor agents and at the same leaves unaffected the mechanism of dilatation Bu has been observed that vasodilatation caused by co the perfused hind limb of a cat is abolished by so cyanide [7], that iodoacetic acid prevents reactive h æmia and dilatation due to nitroglycerin [8], and the sensitivity to acetylcholine of the vessels in a perf rabbit's ear, and the synthesis of acetylcholine, are decreased by complete sympathectomy of the vessel

The mechanism of dilatation, it seems, depends metabolic processes in the vessel wall, and any ups these processes will disturb the mechanism Some upset, we believe, is responsible for the absenc vasodilatation in Raynaud's syndrome

Institute of Industrial
Hygiene, Budapest. L MAG
G OKO

## AN UNUSUAL CASE OF SHINGLES

SIR,—Herpes zoster can be a difficult enough pro in the emotionally healthy patient, but when the dition occurs in a neurotic patient the interval (us a few days) between pain and rash may be an embar ing time for the doctor

A patient of mine, a man of 59, who is prone to ne symptoms, complained of pain in the right lower ches hypochondrium There were no abnormal signs—wh the usual finding in this case The pain persisted and gat strength for the next eight and a half weeks, during time he had repeated examinations by me, he consul naturopath, and finally saw a surgeon who ordered a graph of the chest and a cholecystogram, which were normal Neither the surgeon nor I could be drawn the diagnosis, though the naturopath had a shot at cystitis

The doctor patient relationship gradually worsened approximately sixty one days after the first consult when a characteristic herpetic eruption appeared distribution of the pain

The illness had not yet exacted its full toll, as the lesion and the post herpetic neuralgia incapacitated hi a further fifteen weeks

London S E 26 R N JACKS

## VENEREOLOGY AND DERMATOLOGY

SIR,—We note with concern the advertisement you published for the South East Metropolitan Reg Hospital Board on Dec 18, concerning a vacancy for sultant combining the two specialties of venereolog dermatology This follows a similar appointment was made some months ago by the East Anglian Reg Hospital Board These two special subjects hav points of contact For a number of years general p has favoured dissolution of a union which has no to recommend it beyond administrative conven and which, when it was common practice, aff adversely the standards of both subjects

As the result of this policy, which we comm registrars who have been appointed to departmen venereology or dermatology are being trained as sp ists in their respective fields and have had no opport of acquiring specialist knowledge of the other sub As the result they are ineligible for the appoint which you advertised

We suggest that the institution of such a com appointment is a retrograde step which is unfair to men and women working in these subjects and must ably to inferior standards of work in one or other st depending upon who is appointed to the vacancy it seems highly undesirable that these considerations d be regarded as less important than *administrative* nience

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[1] Lewis T *Heart* 1930 15 177
[2] Lewis T *Ibid* 1929 15 7
[3] Hertzman A B Roth L *Amer J Physiol* 1942 136 669
[4] Greenfield A D M Shepherd J T *Clin Sci* 1950, 9 323
[5] Duff R S *J Physiol* 1952 117 415
[6] Magos, L Okos G *Acta med hung* (in the press)
[7] Pappenheimer J R, Eversole, S L, Soto Rivera *J Physiol* 1948 155, 458
[8] Issekutz B jun Lichtneckert, L, Gáspár Németh Z, He G jun *Acta physiol hung* 1951 2 381
[9] Burn J H *Physiol Rev* 1950 30, 177
[10] Armin J Grant R T, Thompson, R. H S *J Physiol.* 121 603

AMBROSE KING
BRIAN RUSSELL.

London Hospital E 1

## SALARY AND LEAVE SCALES

,—I wonder why it has just been decided to fix ) as the salary point at which hospital medical can claim six weeks' leave I notice the new scale come into force as from April 1 1955 As I received atest increment in October putting me at £1025 now have to wait till next October before I can claim weeks' leave ? Why has the reputable figure of ) now been withdrawn ? I can see no reason for g on the higher figure of £1050 Is this just another of officialdom at the expense of junior hospital cal staff ?

ton, Surrey J B GURNEY SMITH

## STREPTOMYCIN WITHOUT TEARS

r,—Those of us who have to treat tuberculous chil are often upset at the distress caused by a daily tion of streptomycin given over a period of months ar ago we started to give these injections routinely hour after the child had fallen asleep with most factory results.

e efficacy of this method is well shown by the small who started with daytime injections and then ged to the nightly routine When I pointed to some it puncture marks on his thigh and asked what they his answer was Oh that's where I *used* to have pricks

others are not using this method they should at give it a trial

Thomas's Hospital
London S.E 1

M. PICKERING PICK

## CANCER OF THE LUNG

R—On Feb 12 last the Minister of Health in a ten answer, stated he had received advice from the ding Advisory Committee on Cancer and Radio apy on the question of the relationship between king and lung cancer In his statement the Minister ared that it must be regarded that there is a relation and that there is a strong presumption the relation is causal He added that other factors may be ating—e g., atmospheric pollution—and that it is rable that young people should be warned of the risks arently attendant on excessive smoking and that it ld appear that the risk increases with the amount ked particularly of cigarettes

his report on the State of the Public Health in 3 the chief medical officer of the Ministry of Health ribes the inexorable march of cancer of the lung as ysterious May I suggest that this description is leading and is apt to discourage those who have ence with the community from giving the advice ffered by the Minister to young people

ranted that the specific carcinogenic factor has not n isolated as yet there is no real mystery associated h a condition *that in 1953 was responsible for 27%* ll male deaths from cancer

ouse of Commons
London S W 1

BARNETT STROSS

IR —May I support Dr Joules's plea in your Christmas y issue for honesty in facing the implications of the parently causal relationship between cigarette smoking l cancer of the lung ?

The community suffers from a mass addiction to the g of tobacco and is bombarded with advertisements *all those with an interest in maintaining this addiction* We are ill served by the chief medical officer, who may be regarded as the High Priest of Preventive Medicine, if he suggests in an official report that the cause of lung *cancer is akin to the mysteries of religion* The *march of* this disease will certainly be inexorable if the interests of the tobacco trade and the revenue are allowed to obscure the authoritative warning that should be given to the public

Barnet, Hertfordshire DOUGLAS MCCLEAN

# Parliament

## QUESTION TIME

### End of Agene

Replying to a question Mr HEATHCOAT AMORY Minister of Food said that he had now received a report from the subcommittee set up under the chairmanship of the chief medical officer of the Ministry of Health, to consider flour improvers A detailed experimental study had been made under the Medical Research Council The methods of flour improvement which had been examined were agene chlorine dioxide, potassium bromate ascorbic acid, and an aeration *process.* The experiments had confirmed that agene treated flour when fed in large quantities caused fits in dogs and had shown that none of the other improvers tested did the same Since other methods of flour improvement existed which had not produced these symptoms in animals the Government were of the opinion that, although no ill effects in man due to the use of agenised *flour* had been established effect should now be given to the decision taken in 1950 to discontinue agene

In view of this decision the National Association of British and Irish Millers had agreed to recommend their members to discontinue the use of agene and to give an undertaking that the equipment for treating flour in this way would be removed from their mills by December 31 1955 Some delay was inevitable because new equipment had to be obtained to treat flour by other means. The National Association of Flour Importers had similarly agreed to recommend their *members to ensure that no flour treated with agene would* be imported by them.

The further investigations undertaken by the Medical Research Council had revealed some differences between the effects on flour of the other methods of improvement but the effects demonstrated were not sufficient to require the discontinuance of any of the other flour improving processes. These methods of flour improvement would continue to be kept under close scrutiny in collaboration with the milling and baking industries.

### The Case of Mrs Christofi

Replying to questions on the case of Mrs Christofi Mr GWILYM LLOYD GEORGE the Home Secretary said that Parliament had on many occasions recognised the undesirability of pressing the Home Secretary to disclose the reasons why he did or did not tender advice to the Crown with regard *to the exercise of the prerogative of mercy in a capital case* The principal medical officer of Holloway prison had stated in a report dated Oct 5 1954 that he had formed the conclusion that Mrs. Christofi was insane but was medically fit to plead and to stand trial A copy of that report was furnished to the defence

In view of this report he had appointed three distinguished and experienced doctors to conduct an inquiry in accordance with the law The three doctors reported that the prisoner was not in their view insane and they added that in their view she did not suffer from any minor mental abnormality *which would justify them in making any recommendations* on medical grounds relevant to the question of a reprieve

After full consideration he came to the conclusion that there were no sufficient grounds for interference with the due process of law It would be contrary to long-established practice and as he thought open to considerable objection to disclose any advice tendered to the Home Secretary in a case of this kind by the trial judge or to disclose the terms of the medical report submitted by the statutory inquiry and he was not prepared to make these documents available There was no electro encephalograph examination of Mrs. Christofi as she would not agree to the examination being *made*

### Clinical Experiments at Hospitals

Replying to questions, MISS PATRICIA HORNSBY SMITH, parliamentary secretary to the Ministry of Health, said that hospital authorities were given power to conduct research by section 16 of the National Health Service Act, 1946 Individual clinical investigations were undertaken on the authority of the clinician in charge of the case, and the Minister had not complete knowledge of the extent of all the work in progress at hospitals Such investigations involved medical and ethical problems which were not susceptible of control by regulations

### Refunds of Prescription Charges

Replying to a question, MR OSBERT PEAKE, Minister of Pensions and National Insurance, said that from Oct 1, 1953, to Sept 30, 1954, the National Assistance Board refunded rather more than $9^{1}/_{4}$ million shilling charges for the dispensing of prescriptions A small number of these refunds were made to people not receiving a regular weekly National Assistance grant

### Monopack Hearing-aids

Replying to a question, MISS HORNSBY SMITH said that large scale clinical trials of a new 'Medresco' model, capable of being used in either monopack or duopack form, were to be held in the New Year with the coöperation of schools for the deaf and partially deaf If these proved successful, it ought to be possible to begin mass production about the end of 1955 It was proposed to supply miniature batteries for use with the aid in its monopack form free of charge for children, but adults who wished to use the aid in this form would need to buy batteries for themselves They would, of course, still be able to obtain the larger batteries without charge

### Mass Radiography

Replying to a question, MISS HORNSBY SMITH said that up to the end of 1953 the 68 mass radiography units had made 13,396,538 examinations, in about 5% of which some abnormality, not necessarily requiring treatment was revealed

### Orthodontic Treatment for School-children

MR ANGUS MAUDE asked the Minister of Education how many orthodontic specialists were available, full or part time, for the treatment of children in England and Wales under the school dental service —SIR DAVID ECCLES replied There were the equivalent of 17 full time officers, employed exclusively on orthodontic treatment, in the school health service on June 30, 1954, the latest date for which information is available This is an increase of the equivalent of 4 full time officers in the last two years The majority of school dental officers undertake some orthodontic treatment

### Hospitals and Dental Treatment

MISS HORNSBY SMITH replying to a question, said that the work being done by all grades of hospital dental staff, other than house officers, at Dec 31, 1953, was the equivalent of 3803 sessions weekly The total number of beds allocated to consultant dentistry at that date was 249

### Pulmonary Tuberculosis among Student Nurses

MR SOMERVILLE HASTINGS asked the Minister what percentage of student nurses in their first year developed pulmonary tuberculosis in 1953 —MISS HORNSBY SMITH replied I regret that this information is not available

### Birth-control in the Colonial Territories

MR T REID asked the Secretary of State for the Colonies in which of these Territories any system of teaching birth control to the people had been established —MR A T LENNOX BOYD replied So far as I know, no Colonial government has established any such system, but voluntary organisations are at work in some Territories, and in Singapore a government grant is made to such an organisation

### Industrial Health

Replying to a question MR HAROLD WATKINSON, parliamentary secretary to the Ministry of Labour, said that the advisory committee on industrial health would be an advisory body The scheme for the development of industrial health services including any necessary surveys, would be carried out through the Factory Inspectorate which possessed wide powers under the Factories Acts

# Public Health

### Lead Poisoning in Rotherham

ON Dec 20 the medical officer of health for Roth
Dr J A Gillet, was told that two twin boys of 3
Rotherham, admitted to the Children's Hospital, Shef
that morning, had been diagnosed as suffering fro
poisoning He also learned that a younger brothe
had died in Rotherham General Hospital on Dec 1
cause of death being given, after a post-mortem ex
nation, as status epilepticus due to idiopathic epile
He got in touch with the family doctor and heard
details of the history of the three cases Arrangem
were then made for the inspection of the area where
children lived by members of the staff of the Rother
health department It was found that old vul
car-battery cases were being used for fuel in some ho
It seemed that a scrap-dealer, after removing the
plates, was either selling or giving the cases away
nearby residents

Dr Gillet and members of his staff visited the home of
three children and found the grandmother, together
son and a younger married daughter and her baby, at
The old lady, who was edentulous, anæmic, and con
complained of a metallic taste in her mouth The son
no symptoms, but there was a suspicious blue line on
gums The daughter and her baby had no signs or
of lead poisoning In the meantime the chief sanitary insp
had found old battery cases in the coal house and had
told that they were burning them for fuel Samples of
cases and of the resultant ashes were taken for examinati

The police arranged to broadcast a message warning
holders not to burn any car-battery cases, and further
was obtained from the local press

During a house to house visit in the district, the n
and addresses were collected of all the occupants of
where vulcanite cases had been burnt The source of sup
the cases was stopped

It was then learned that a child of 5 who lived in
same area had died on Nov 21, the cause of death
given as cholæmia and infective hepatitis Arrang
were made for two brothers of this child to be
and they were later admitted to hospital suffering
lead poisoning

In view of the danger of lead encephalopathy,
has a far more serious effect on children than
poisoning on adults, it was decided to concentrate at
outset on the children in the affected district A
ments were made with the pathologists of the Pu
Health Laboratory, Sheffield, and of the Mo
General Hospital, Rotherham, to take a blood-count
film of all children exposed to risk, and this inquiry
on Dec 23 Up to the present 127 children and
adults from 41 houses are known to have been expo
The arrangements for blood tests are being cont
the hospital On Dec 22 medical officers from the he
department visited the affected houses and examined
adults, where necessary blood tests were arranged.
circular to all medical practitioners in the district was
out by hand on Dec 22 informing them of the outbr
and of the arrangements made for the examination
suspected cases

As to the disposal of the ashes and old cases, it
happened that the house refuse was collected from
affected district on Dec 21, and a considerable am
was therefore removed A special collection was org
as a further precaution and over 3 tons of cases and
were collected and removed on Dec 22

The lead may have been absorbed through the
(an unlikely route), by inhalation of ash or fumes
off by the burning cases, or by ingestion of food
taminated by dust and by handling the casings and
taminating food with unwashed hands Some of
younger children may have sucked a piece of the ca
Further investigations are proceeding

### Third Quarter in Scotland

In the quarter ended Sept 30, 1954, the inf
mortality rate of 24 per 1000 live births was the l
yet recorded in Scotland, and 8 below the five-
average Neonatal deaths numbered 16 per 1000

ths, 8 less than in the corresponding quarter of 1953 e birth rate was 17·7 per 1000 population—0·4 below e five-year average. Stillbirths amounted to 20 per 00 total births The death rate (10·3 per 1000 popu ion) was 0·2 above the average Deaths from tubercu sis amounted to 17 (respiratory 15) per 100 000 pulation compared with 21 (18) in the third quarter of 53 and a five-year average of 36 (31) There were 206 aths from malignant disease per 100 000 population— more than in the corresponding quarter of 1953 and above the five year average

## Obituary

### ELIZABETH CASSON

O.B.E., M.D. Brist., D.P.M.

Dr Elizabeth Casson, founder and for many years irector of the Dorset House School of Occupational herapy died in Bristol on Dec. 17

She was born in 1881 the third daughter of the late ajor Thomas Casson of Denbigh and she was a sister Sir Lewis Casson She was educated at St. Mary's ollege, Paddington and later studied housing management In 1908 she joined Octavia Hill's stalwart helpers Southwark and seemed to have found her life's work But conditions in South London showed her all too clearly that her tenants, as well as their tenements, needed repairs At the age of 30 she surprised her friends by taking her matriculation and beginning to study medicine

She graduated M.B. in 1910 and soon afterwards joined the staff of the Royal Holloway Sanatorium, Virginia Water In 1922 she took her D.P.M. and in 1926 she proceeded to her M.D. degree. In 1927 she was awarded the Gaskell prize

She herself has described how she came to realise the impor ance of occupation as a form of therapy

I found it difficult to get used to the atmosphere of ored idleness in the day rooms at the mental hospital. hen one Monday morning when I arrived at the women's ards, I found the atmosphere had completely changed and alised that preparations for Christmas decorations had egun The ward sisters had produced coloured tissue paper nd bare branches, and all the patients were working happily groups making flowers and leaves and using all their rtistic talents with real interest and pleasure I knew om that moment that such occupation was an integral part f treatment and must be provided

At Holloway Sanatorium she found a tradition of rafts and games entertainments, sports exhibitions ere all held regularly But it was all voluntary and no ork was prescribed by the medical staff On a visit o the Gart Naval Hospital in Glasgow she saw real occupational therapy for the first time in Dr (now lr) David Henderson's small department. Later she isited the larger department at Bloomingdale Hospital n New York She continued to seek out all the hospitals n England where the idea was gaining ground including ayland Sanatorium and the Lady Chichester Hospital in righton In 1929 she left Virginia Water to open a esidential clinic at Dorset House on Clifton Down near Bristol She was determined to arrange a full time lanned day for all her patients, and from this grew the Dorset House School of Occupational Therapy Soon fterwards a small department was opened at the Bristol eneral Hospital to show how occupational therapy ould also be used for patients with physical diseases.

The work continued to develop steadily and in 1936 he inaugural meeting of the Association of Occupational Therapists was held at Dorset House Shortly before he war the staff of the school helped in the planning nd opening of the Allendale curative workshop and Dr Casson reported in our columns in 1941 on the first 40 cases treated there (*Lancet*, 1941 ii 510)

With the war Bristol became an unsuitable place in which to run a school, and after some months of anxious negotiations Dr Casson arranged for her students to move to Barnsley Hall Hospital Bromsgrove After the war the school found new quarters at the Churchill Hospital in Oxford but Dr Casson continued to act as medical director and paid frequent visits from Bristol In 1951 she was appointed O.B.E.

F. S. C. writes: The memory of Elizabeth Casson will be cherished not only as an able psychiatrist and charming colleague, but also as the founder of the first school of occupational therapy in this country Soon after the late Sir Robert Jones had demonstrated the value of the curative workshop, she saw the need for trained personnel and recognised that, besides a knowledge of suitable crafts, the therapist must understand the nature of illness and how work therapy could help patients with both mental and physical disorders back to health From her own resources she established the Dorset House School of Occupational Therapy and sustained it by her teaching forthright leadership, and generosity throughout the difficult period of evacuation and expansion during the war until it was safely established under an independent board of governors of which she was a member Occupational therapy today owes a great deal to the foresight and example of Elizabeth Casson

### WILLIAM JOHN HANDFIELD HASLETT

Kt., M.R.C.S., J.P.

Sir William Haslett, who died on Dec. 17 at Weybridge, was for many years a valued member of the Middlesex County Council. His public service was inspired and directed by his medical training and experience and as chairman of the council's committee for the care of mental defectives he was actively concerned in setting up colonies for the mentally handicapped

He was born in Donegal in 1866 the son of Dr S Torrens Haslett of the Colonial Medical Service. He was educated at the Academical Institute Londonderry Trinity College Dublin and the London Hospital After qualifying in 1889 he held resident appointments at the Poplar Hospital and St. Luke's Hospital for the Insane and a clinical assistantship at the National Hospital for Paralysis and Epilepsy In 1892 he became proprietor and medical superintendent of Halliford House a private mental hospital at Sunbury-on Thames

Soon after he settled at Sunbury he was elected to the Staines board of guardians, the Middlesex insurance committee and the Sunbury urban council. All these interests were a preparation for his work on the county council *He was also a justice of the peace for Middlesex* He was created a knight in 1938 for his public services.

Sir William married in 1922 Norah daughter of Mr W. A. Macan She survives him with a son and three daughters.

## Appointments

ELLIOT, MARGARET M., M.B. Sheff.: school M.O., Sheffield.

GHOSH, A. K., M.B. Calcutta, D.OBST.: registrar in obstetrics and gynaecology, Peterborough Memorial Hospital

KELLY, J. F., M.B. N.U.I., D.P.H.: asst. M.O., British Railways (London Midland region)

MCGRATH, S. D., M.R.C.P.I., D.P.M.: resident medical director, St John of God Private Psychiatric Hospital, Stillorgan, co. Dublin.

MORGAN, J. D., M.B. Sheff., F.R.C.S.: consultant orthopaedic surgeon, Wingfield Morris Orthopaedic Hospital, and accident service of the United Oxford Hospitals

PAUL, JACK, M.B. Witwatersrand, D.C.H.: appointed factory doctor, Tottenham, Middlesex.

PORTER, K. R. D., M.B.E., M.R.C.S., D.P.H.: deputy senior administrative M.O., Oxford R.H.B.

PUGH, R. C. B., M.D. Lond.: whole-time clinical pathologist, St Peter's, St Paul's and St Philip's Hospitals, London.

WILLIAMS, J. H., M.B. Lond.: asst. M.O., British Railways (London Midland region).

South Western Regional Hospital Board:

EARLE, B. V., M.D. Dubl., M.R.C.P., D.P.M.: consultant psychiatrist, Exeter clinical area

MOORE, H. D., M.B. Sydney, F.R.C.S., F.R.C.S.E.: consultant surgeon, Exeter clinical area.

PAYNE, J. W., M.B. Manc., F.R.C.S., D.O.M.S.: consultant ophthalmologist, Plymouth clinical area.

Amended notice.

# Notes and News

## THERAPEUTIC SUBSTANCES

THE Therapeutic Substances Act, 1925, has been amended to include within its schedule parenteral preparations of oxytetracycline, and the Therapeutic Substances Regulations, 1952, have been amended to include methods of preparing this drug[1] Oxytetracycline is removed from the list of substances which may be sold only on the prescription of a doctor, dentist, or veterinary surgeon[2] More up to date regulations for insulin preparations are approved[1] Erythromycin, neomycin, oxytetracycline, polymyxins, cortisone, corticotrophin, and hydrocortisone are added to the substances controlled by the Penicillin Act, 1947[3] All these measures come into operation on Jan 1

## DISORDERS OF INFANCY

AT a meeting of the Devon and Exeter Medico Chirurgical Society on Dec 16, Dr F S W Brimblecombe spoke of some common disorders of childhood It is a sombre thought, he said, that if the human female had always carried out efficiently her natural function of lactation there would have been no problems of infant feeding, uncountable millions would not have died in infancy, and the whole history of the human race might have been changed It is only during the past half-century that we have had anything approaching an efficient substitute for breast-milk or hygienic methods of artificial feeding

Underfeeding is common, overfeeding very rare If a baby fails to thrive it is wise to seek the cause in the baby rather than in the feed A baby who screams on being fed should be examined for an anal fissure The word marasmus is now obsolescent Most of the causes of failure to thrive can now be recognised Wrong feeding is one, but a rare one Another is hiatus hernia, here the function of the cardiac sphincter is lost and the patient vomits from birth especially when laid flat The vomit contains mucus and sooner or later, owing to œsophageal ulceration, blood Painful swallowing from the same cause produces anorexia, and occult bleeding may give rise to anæmia The diagnosis is a clinical one, for confirmation by radiography is difficult Feeds should be thickened and the baby sat upright To free a stomach which has ridden up into the chest and become adherent surgery is occasionally required.

Bottle fed babies, apparently thriving, sometimes start to vomit at the third or fourth month, become costive, and develop unexplained pyrexias These infants need not die Necropsy reveals calcification in the proximal renal tubules This calcification is radiographically demonstrable during life In these cases, first described by Dr Reginald Lightwood, there is acidræmia with a urine constantly alkaline This disorder, persistent renal acidosis can be treated successfully with large doses of sodium bicarbonate In another group, clinically similar there is hypercalcæmia of unknown origin which is equally controllable by a calcium free diet

Infants are occasionally poisoned accidentally by the too liberal application of boric powder to raw buttocks Boric poisoning causes a generalised rash which desquamates, diarrhœa and vomiting, and perhaps coma and death Infants who suck or gnaw at their cots which have been painted with lead paint occasionally develop lead poisoning In infancy plumbism manifests itself in pallor, abdominal pain, drowsiness and convulsions Radiography shows a lead line round bones, but there is no polyneuritis and blood changes are absent Circumcision, which is responsible for sixteen deaths annually, is justified only in infants who cannot pass urine A tight prepuce—and tongue tie—are physiological states in infancy

## A NEW OUTPATIENT DEPARTMENT

BETWEEN 1935 and 1948, outpatient attendances at St James' Hospital Balham, rose from 30,000 to well over 100 000 annually, and the need for an enlarged outpatient department became urgent The new building, which is now in use, is a notable example of imaginative hospital planning The design s pleasing features include a large and beautifully furnished lounge for visitors or waiting patients, a pram store conveniently situated near the postnatal clinic and two automatically operated stretcher lifts, fitted with levelling devices All internal structures have been
to allow alterations to be made quickly and easily
transverse partitions may be removed and re-erected
where within a matter of minutes, and all cubicles
examination rooms have interchangeable electrical
To enable patients to find their way about, each depart
has its own colour scheme, and the hospital proposes t
appointment cards in corresponding colours Noise in c
is kept down by perforated "acoustic" boards in the c
and the floors are made of cork tiles Door handl
designed for elbow action All furnishing fabrics
pleasantly harmonious patterns, and particular att
has been paid to comfort and utility in designing the cons
room furniture The aim has been to evoke an atmo
at once sympathetic and quietly cheerful, as well as to p
for functional efficiency

## OVERWEIGHT AMERICANS

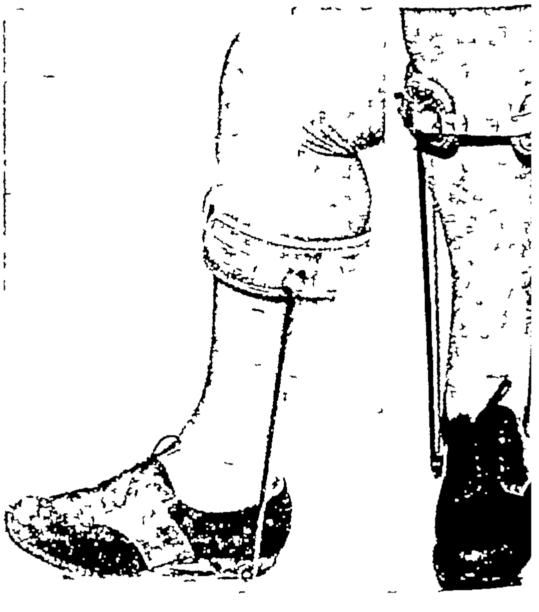
THE United States Army in Europe, worried by the n
of stout people in its ranks, is urging its plumper s
to get their weight down Back home, it seems, thin
much the same, for a report[1] now suggests that mor
20% of the population of the United States are overw
"Overweight" was defined as 10% or more abov
"desirable" weight for the individual, which was bas
measurements of height, weight, and build or body typ
Metropolitan Life Insurance Company has constructed
of desirable weights that show a range of weights fo
inch of height by type of body frame) Of the over
population, round about 10% were 20% or more above
desirable weight, and there was a relatively higher prop
of Negro females in both the 10% and 20% overw
categories

## A LIGHT SPRING CALLIPER

Mr G Douglas Nickels, M C S P, remedial gymn
Mount Vernon Hospital, Northwood, Middlesex,
The accompanying photograph shows a new light
calliper that has been used in the department of p
medicine at Mount Vernon Hospital for the last three
It has been developed primarily for the hemiplegic
but has been used successfully on other patients with
foot" The advantages of this type of calliper are

(1) Light weight It weighs about 9 oz
(2) Ease of fitting It can be fitted by the physiotherapist
department
(3) Low cost It costs about 15s

The calliper is made in three sizes to fit different size
It is $13\frac{1}{2}$ in long and measures $3\frac{1}{2}$–4 in under th
It is wound from 6 and 8 B I S gauge wire. The side
are joined at the top by a stiff leather band with str
buckle



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[1] The Therapeutic Substances Amendment Regulations 1954
[2] The Therapeutic Substances (Supply of Oxytetracycline for Agricultural Purposes) Regulations 1954
[3] Therapeutic Substances (Control of Sale and Supply) ulations 1954

[1] *Publ Hlth Rep Wash* 1954 69 1084

For fitting the heel of a good lace up walking shoe is illed to take a ¼ in steel peg This acts as the fulcrum, id makes a firm attachment for the spring Inversion can corrected by drilling the hole at an angle dependent on e degree of correction required The calliper is then sprung n to the projecting ends of the peg The calliper is not tended to be a 90% foot stop but it is a spring designed to lp the patient to lift his foot when walking

## THE SCALPEL, THE SWORD

This title has been given to an emotional biography of orman Bethune a Canadian surgeon[1] In 1927 he was ying of pulmonary tuberculosis in a famous New York anatorium There he read of a wonderful new cure for his isease—artificial pneumothorax. He demanded the treatment and was cured. Later he became a skilled thoracic urgeon, but he threw up his career on the outbreak of the panish civil war and went to Madrid to help the anti Fascist orces. When the war ended he returned to Canada and oined the Communist party But his turbulent spirit called or something more exciting than civilian practice: the hinese people were fighting against invasion and there was n urgent need for doctors Early in 1938 Bethune left ancouver for Hong Kong taking with him enough equipment nd supplies to fit up several surgical units He reported o Mao Tse-tung who welcomed the suggestion of a mobile perating unit close to the front Bethune seems to have lone remarkably good work under very difficult conditions ut towards the end of 1939 he contracted fatal septicæmia rom an infected operation wound This biography carries he recommendation of the Book Society and will probably e widely read. Doctors may not be wholly convinced by he publisher's claim that "No doctor not Hippocrates nor Jenner nor Pasteur nor Sir Alexander Fleming is known and enerated by as many people as Norman Bethune

## AUTOMATIC AMPOULE INJECTOR

This indefatigable Sir Christopher Wren somehow found ime in the midst of his more widely known pursuits, to nstruct one of the earliest practicable syringes. His iginal model[2] which he used experimentally on dogs, onsisted of a hollow quill attached to a bladder containing the uid for injection and in 1656 he wrote: I am in further ursuit of this experiment which I take to be of great concernent and which will give great delight to the theory and ractice of Physick. Three centuries have passed since en, and the technique of injection continues to evolve he latest of many refinements are incorporated in the evice known as the Ampin[3] which is an automatic mpoule injector for routine and emergency hypodermic jections. In America it was first demonstrated at the merican Medical Association convention at Chicago in 1948 t consists of an ampoule of the solution for injection, under ressure of an inert gas, connected by flexible transparent tub ng to a needle with a glass cover To make an injection the over is removed and the needle inserted into the selected ite with the usual antiseptic precautions. (If a vein is accidenally entered, blood will flow into the tubing when this is inched and released) The tip of the ampoule is then snapped y bending the transparent tubing and the pressure of the as forces the solution through the needle The whole rocess, it is claimed is considerably quicker than ordinary ethods of injection, and in addition it ensures accuracy of osage and maximum sterility Syringe transmitted hepatitis avoided since each ampin is used once only—which ncidentally means that patients have a sharp new needle for ach injection The possibility of glass fragments passing own the needle has been investigated and we understand hat the risk may be discounted The method is specially uitable for general practitioners, district nurses, and mid ives, and the ease of administration will be attractive to usy anaesthetists Intravenous infusions of saline and plasma an also be given in the same way

The British representatives say that the ampin is actually heaper to use than the traditional syringe Preliminary gures which they have obtained from hospitals with a central yringe service indicate an over-all cost including maintenance and renewal of about 9d. per injection One ampin, on the other hand can be bought by hospitals for rather less than 7½d; and the labour and expense of servicing are of course eliminated Both these figures are exclusive of the cost of the the drug

The manufacturers and distributors in this country are Curzon Gerrard & Co Ltd Fountain Lane Oldbury Birmingham.

## FILMS ON DENTAL EMERGENCIES

Most medical graduates are required to enter one of the three Services shortly after registration and sooner or later many of them—particularly those who join the Royal Navy—find themselves dealing unaided with dental emergencies For this reason the Admiralty has issued a series of colour films and film loops which show in detail the measures which may be used to tide patients over until they can be seen by a dentist

Three of the longer films describe dental inflammatory conditions, operative techniques (including local anæsthesia and the treatment of postoperative pain and bleeding) and the management of injuries to the teeth and jaws. Nine short film loops in colour have also been prepared each showing the extraction of a tooth. All illustrate clearly by means of diagrams models and practical demonstrations, the essentials of diagnosis and treatment of inflammatory and traumatic dental lesions. The commentaries are good the exposition is unhurried and important details are suitably emphasised.

These films were designed originally for Naval doctors, but the Admiralty suggests that they might also be helpful to senior medical students. The films will shortly be available for hire or purchase from the director of Naval training at the Admiralty

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### University of Birmingham

On Dec 17 the following degrees were conferred:

*Ph.D (in the faculty of medicine)*—D M Edward

*M.B Ch.B*—Yaw Asirifi, P H Artill Joyce E Bailey Patricia A. Bramley John Bullock, E P C. Hadley Olga R. Harbron Ella E. L. Holt J W P Jarrams, David Learmont A P Mayne, E. T Molloy, W K Merifield, Kenneth Middleton J D Nicholas P A North, L J T Pearson, A Sutherland, Elizabeth M. Tilsen Derek Wright R. A Yeomans

### University of Bristol

In recent examinations the following were successful:

*M D*—A. G W Branch.

*M B Ch B*—H T Apsimon, Pamela M. Atkinson, I H Barry Catherine A Clark K G Collins D J C. Felton J H L Criffin M L Harvey J K Howell Antoinette R. Joseph, J McC Laitoo Jean D Matthews T N Matthews J H Orr B K Palmer B A. Poley E O Skeens

### University of Durham

On Dec 18 the degrees of M B B.S. were conferred on the following

A L. Brown P J Burnett, Mary Campbell Fook Kwee Chai J R. Clark, J F Colville G S Cowin, Joan A Davison Francis Duran Florence Farrow J F Fenby A L Ferguson, William Granger C. B Hackett, Susan E. A Hart, N C Haswell G. A Nutt Bridget A W Osselton, Sydney Phinn P F W Rowell Jean C Russell Elizabeth J Studdy Foster Thompson B R. Tindle, S V J Watson Pamela Willis

In absentia.

### University of Liverpool

At recent examinations the following were successful

*M D*—E F B Cadman, B R Frisby S. Gillis G Hughes, D E. Paterson, G W Storey E H Wilson.

*M Ch.Orth*—B S Jones M. A Vail

*M B Ch.B*—J D Agnew, J A Barlow, I K Brown, B J Charlick G O Dubourg T R. Evans Patricia O Grundy I A Harrison T R. T Hughes, R. A Johnson J L Mason W V S Pugh, Mary F Shepherd D Taylor Robinson R. A Yorke

*D M R T* (Part II)—J K Ganguli

*D T M & H*—B A Chaudhary, J Ghosh, June H Green B A Johnson A J Jones G P Lowther M. L. Magotra, A M Maldon, H C Onyeabo D J Patel B Prasad, C I Somaya, J K S Yearsley

The Milne medal in tropical medicine has been awarded to Dr G P Lowther

### Royal Faculty of Physicians and Surgeons

At a meeting of the council on Dec 21 with Prof Stanley Graham, the president in the chair the following were admitted to the fellowship:

Jasoda Jiban Das, J A Rundle W C Watson

### Royal Society

Locke research fellowships have been awarded to

Dr M de Burgh Daly to work on carotid sinus reflexes and hæmodynamics of the pulmonary circulation, at University College London

Dr J C F Poole to work on the effects of fat absorption and blood coagulation and thrombosis, at the Sir William Dunn School of Pathology Oxford

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[1] The Scalpel, the Sword The Story of Norman Bethune By SYDNEY GORDON and TED ALLAN London Robert Hale 1954 Pp [illegible] 16s.

[2] Gottfried O A F [illegible] September 1953

[3] Batterman R. C Rovenstine E. A *J Lab clin Med* 1950 35 795

## University of Sheffield

Mr O Daniel has been appointed senior lecturer in surgery, and Dr D Balducci research assistant in bacteriology and virus diseases

## University of Edinburgh

On Dec 17 the following degrees were conferred

*M D*—G S Kilpatrick * J W Lusk, † G M Maxwell
*Ph D (in the faculty of medicine)*—A. N George, Sourindra Mohan Ghosh I A Macpherson, D I Nisbet
*M B , Ch B*—A J Bennet A A H Brown, J A Brown, C F M Caird, P G Coffey, R W Davidson H P Davie G F Davis, P G Drummond Smith, W D Fanner Alan Ford Hunter, D A K Goldenhuys H C R Hinwood P Y Kyle M H Lea, Kian Poen Lim A G Mackinnon D G Mochie, Denis Moore * Sheila M L Moore, D R Oliver, W F Parrott, Shirley A Peacock, W H Rable, J L Smith, A. T Thomason, R A P Whitelaw, John Wood, I F Young

* In absentia † Highly commended

The following diplomas have been awarded

*D P H*—D F Baxter
*D M.R D*—W N Boyd, R F Cant, J H Greig A H Morris A A Wild
*D Psych*—J G Henderson, P J Zeck

The George Guthrie research fellowship in child health was awarded to Dr J F J Collins, and the Hastilow research scholarship in rheumatism was awarded to Dr W R M Alexander

## Royal College of Surgeons of Edinburgh

At a meeting of the college on Dec 15, with Prof Walter Mercer, the president, in the chair, the following were admitted to the fellowship

W A Baker, G T F Braddock, Guru Kripa Chaudhuri J N de Klerk, C J Dewhurst J B Doss, J M du Toit, Mourad Mahmoud El Fiki Harry Fine, W D Graham J J Ironside A J A McCormick, G T Mair K P P B Menon, M J Meter Durga Prasad Misra G F Murnaghan, Bhalchandra Vasudeo Nabar Jagdish Swarup Pathak, James Piggot, Nukalapati Balakrishna Reddy, W C Robinson Roy Shree Krishna, Pramod Karan Sethi, Gajendra Sinh R. G D Taylor

## Royal Sanitary Institute

Fellowships have been conferred on

Dr J C R. Buchanan Colonel P J L Capon Dr Archibald Dodd, and Dr William Hogg

## University of New Zealand

Mr H M Carey, who has been acting professor since Prof Spence Smyth resigned early this year, has been appointed to the postgraduate chair in obstetrics and gynæcology at Auckland University College The appointment carries also the medical directorship of the National Women s Hospital under the Auckland Hospital Board

Professor Carey was born in New Zealand and graduated M B at the University of Sydney in 1941, having held a part time lectureship in physiology and biochemistry After holding resident posts at the Royal Hospital for Women Sydney and Queen's Park Hospital, Blackburn Lancashire he spent four years as senior registrar in obstetrics and gynæcology at the Postgraduate Medical School of London. He also spent a year in the department of obstetrics at Johns Hopkins Hospital From 1943 to 1945 he served in the R.A A F as officer commanding No 1 Aviation Medicine Section He began work in New Zealand as assistant in the professorial unit early in 1954 He has published papers on the use of ion-exchange resins oxytocics and fœtal distress

## McGill University, Montreal

Dr W Clifford M Scott has been appointed associate professor in the department of psychiatry to organise facilities for training in psycho analysis

Dr Scott graduated from the University of Toronto in 1927 After working under Prof Adolf Meyer and Prof Macfie Campbell, he continued his studies in London at the National Hospital Queen Square and the Institute of Psycho analysis taking the D P M in 1934 He later became director of the Clinic of Psycho analysis in London and during the late war was a psychiatrist in the E M S He is a member of the staffs of the Institute of Psychiatry and of the Bethlem Royal and Maudsley Hospital London He is also an assistant editor of the *International Journal of Psycho-analysis* and president of the British Psycho Analytical Society

## E E G Society

A meeting of this society will be held at 10 30 A M on Saturday, Jan 8 at the National Hospital, Queen Square, London

## London County Medical Society

The annual dinner of this society will be held at the Talbot Restaurant 64, London Wall, E C 2, on Tuesday, Jan 18, at 7 30 P M , when Dr Robert Forbes secretary of the Medical Defence Union, will speak on medical litigation Tickets (11s 6d ) may be had from Dr A M Ramsay, Royal Free Lawn Road, N W 3

## Exhibition of Israeli Scientific Publications

This exhibition, which is being held at the Consulat Israel, 18, Manchester Square, London, W 1, is to open until Jan 7

## Association of Clinical Biochemists

*Southern Region*—The annual general meeting of region is to be held at University College Hospital, Lon W C 1, on Monday, Jan 10, at 3 15 P.M At 4.30 scientific papers will be read

## Institute of Diseases of the Chest, London

Clinical demonstrations on chest disease are given Fridays at 5 P M at this institute (in the grounds of Brompton Hospital, Fulham Road, S W 3) They are without fee to doctors The next series will begin on Ja and end on April 1

## Colonial Work of the N A P T

The National Association for the Prevention of Tubercul has presented to the secretary of State a memorandum on association's activities in Colonial territories Over the nine years this association's work in backward areas h included large scale health propaganda, and the provi of well trained professional teams By means of N.A. scholarships, 55 doctors, nurses, and sanitary workers, fr 18 Colonies, have been enabled to come to Britain for stud The memorandum drew attention to the Colonies' need more tuberculosis specialists and greater research faciliti and indicated the association's willingness to assist t Colonial Office in overcoming the pressing problem of losis among immigrants to Britain from the Colonies.

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CORRIGENDUM *Scottish Appointment*—Dr C J Swan is chairman of the General Medical Services Subcommit (Scotland), and *not* of the Scottish Health Services C as we incorrectly stated last week (p 1336) Captain J Younger is chairman of the council

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Sir Lionel Whitby is to be visiting professor of medicine a New York State University College of Medicine in January

*The Wellcome Historical Medical Museum* has moved f Portman Square, London W 1, to the Wellcome Research In tion, 183 Euston Road, N W 1 Exhibitions dealing with pri medicine and with child welfare through the ages are open to public in the new premises (Monday to Friday, 10–5)

# Diary of the Week

JAN 2 TO 8

### Monday, 3rd

INSTITUTE OF NEUROLOGY, The National Hospital, Queen Sq W C 1
 5 P M Sir Geoffrey Jefferson F R S Benign and Malig Tumours of the Gasserian Ganglion

### Tuesday 4th

ROYAL COLLEGE OF SURGEONS OF ENGLAND Lincoln s Inn Fi W C 2
 3 45 P M Dr G D Lamb *Pathological Aspects of Ulc* Colitis (Erasmus Wilson demonstration )
INSTITUTE OF DERMATOLOGY St John s Hospital Lisle St W C 2
 5 30 P.M Dr L Forman Skin Lesions with Deeper Signific

### Wednesday, 5th

ROYAL SOCIETY OF MEDICINE 1, Wimpole Street W 1
 5 15 P M *History of Medicine* Miss Jessie Dobson Wil Clift Dr Norah Schuster Dr Isaac Buxton
 8 P M *Surgery* Mr H T Simmons Dr C J Gavey Norman Dott Dr G F Abercrombie Palliati Cancer
INSTITUTE OF DERMATOLOGY
 5 30 P M. Dr H Haber *Parapsoriasis Poikiloderma* Mycosis Fungoides
MEDICO CHIRURGICAL SOCIETY OF EDINBURGH
 8 30 P M (Royal College of Surgeons, 18 Nicolson S Dr W I Card Mr John Bruce Ulcerative Colitis

### Thursday 6th

ROYAL COLLEGE OF SURGEONS OF ENGLAND
 5 P M Mr J M Potter Angiomatous Malformations of Brain (Hunterian lecture )
ROYAL SOCIETY OF MEDICINE
 8 P M. *Neurology* Sir Francis Walshe, F R.S The Futu Neurology
ROYAL ARMY MEDICAL COLLEGE Millbank, S W 1
 5 P M Miss Muriel Robertson F R.S Sir David Bru Appreciation of the Man and his Work

### Friday, 7th

ROYAL SOCIETY OF MEDICINE
 5 30 P M *Anæsthetics* Prof E A Pask Maintenan Respiration in Respiratory Paralysis
INSTITUTE OF DERMATOLOGY
 5 30 P M Dr J E M Wigley Psoriasis (Clinical demon tion )
ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASGOW St Vincent Street Glasgow
 5 P.M Dr I Anderson Electrolyte Balance

# MAN AS AN EXPERIMENTAL ANIMAL*

Sir GEOFFREY JEFFERSON
C B E M.S Lond. LL.D., F.R C S F R.C.P F.R.S
ERITUS PROFESSOR OF NEUROSURGERY IN THE UNIVERSITY
OF MANCHESTER

THERE are some branches of research in which man the pre-eminently suitable in fact the only possible bject All have to do with the nervous system and pecially those concerned with sensation with pain and ith thinking

### Experiments on the Brain

The first operation for a brain tumour was performed n Nov 25 1884, and gave rise to discussions in the imes

Someone signing himself F R S' led off on Dec 16 ith a long letter describing in vivid terms what had appened It seemed to him to be a wonderful oppor unity for a telling reply to the Bishop of Oxford and ohn Ruskin who had just spoken strongly against hat was so curiously called vivisection The point bout the famous operation was that the situation of e tumour had been localised to the upper part of the otor area by a comparison between on the one hand e patient s symptoms and signs, and on the other hand e maps of cortical localisation which resulted from the nimal experimentation of the Germans, Fritsch and litzig and more still, of David Ferrier ' F R S., ad a picturesque literary style which you can savour rom the following extract from a very long letter escriptive of the steps of the logical application of perimentally verified facts

> ' While the Bishop of Oxford and Professor Ruskin were somewhat intangible grounds denouncing vivisection at xford last Tuesday afternoon there sat at a window of the spital for Epilepsy and Paralysis in Regent s Park in an valid chair propped up with pillows, pale and careworn t with a hopeful smile on his face a man who could have oken a really pertinent word upon the subject and told the ht Rev prelate and great art critic that he owed his life d his wife and children their rescue from bereavement and y to some of these experiments on living animals which so soundly condemned.

e Bishop of Oxford replied on Dec 19 that if a ct knowledge of the secrets of the human frame is ed in the interests of mankind let mankind be the ns These letters led to a shower of further letters, n Christmas Day mostly in support of F R S R S had to add a further note on Dec 26 saying the poor man was dead (of infection) In a long r on Dec 27 the *Times* took the view that in spite e eventual fatality Rickman Godlee s experimental tion had been fully justified and that the gateway erebral surgery had been opened This was an rtant pronouncement and true Do I need to add on Dec 26 there was a letter from James Whitson tant surgeon to the Glasgow Royal Infirmary saying this was not the first operation on the brain for our, that a Scotsman William Macewen had got first ? Whitson was quite correct. Then letters to vie for place with news of Mr Gladstone s 75th day letters on The state of the business at nisi s and scandalised objections to some undraped es in Alfred Steven s designs for the decorations of dome of St Paul s—designs that had the weighty mendation of Sir Frederick (later Lord) Leighton Mr (later Sir) E J Poynter—men whose artistic g was nearly as high then as that of Velasquez Raphael

So we see that remarkable experiment come and go to lead to more in the fullness of time than *The Lancet* had lugubriously prophesied for it in its leader on Nov 10, 1883 *The Lancet* held that *acceptance of the* laboratory discoveries was not unanimous and that the facts themselves were somewhat confusing (as indeed they were) The leader proceeded

> But it must be confessed that the aid localisation has afforded to treatment has been small and practically confined to cases of surgical interference Even of these cases there are very few—scarcely more than could be counted on the fingers on one hand—in which the power of localising cerebral disease can be said to have been the means of saving a life that would have been lost without it

It concluded with these minatory words

> If Dr Ferrier s suggestions meet with much practical response it is to be feared that cerebral localisation will soon have more deaths to answer for than lives to boast of

These lines were evidently written either by a physician or a pessimist, the author could of course have been both

We see, then that these experiments on man had the mixed reception that we should have expected at that date It required the courage of a man like Sir Victor Horsley and after him Harvey Cushing to silence opposition and to win the confidence of the world.

All operations are of their nature experimental the statistical results are broadly known and from them the general impersonal risks can be calculated In some what concerns us most is danger to life itself in others fatality can be almost excluded and the experimental side depends on the success that can be expected, the relief that can be anticipated in the individual instances No statistics have so personal a message If it comes to that all medical treatment is also experimental As Professor Pickering has pointed out, the prescription even of rest in bed for two or three weeks or of a bottle of cough mixture, are experiments the results of which deserve closer observation and quantitative analysis than they got.

### Sensation

I mentioned just now that man was the only suitable animal for experiments on sensation and on pain It was by regarding closely the stages of sensory and motor recovery after nerve suture that what we call generally sensation was broken down into a number of components (light touch the recognition of pain pressure temperature localisation of the point touched and so forth) It seemed to Henry Head who was deeply *interested in this subject that he would appreciate the* whole thing better if he had some nerves cut in his own left arm This was done by Dean and Sherren of the London Hospital in 1904 Head chose what he thought were purely cutaneous nerves and came to some wrong conclusions by that mistake as J S B Stopford pointed out His other mistakes in interpretation have been pilloried by F M R Walshe The correctness or otherwise of Head's results is beside the present point, which is that he decided to turn himself into his own experimental animal Wilfred Trotter and Morriston Davies followed suit shortly afterwards and arrived at conclusions that have stood much better the test of time Since then the personal experiment has been applied by other research workers.

#### THE PAIN OF CANCER

A constant problem for the neurosurgeon is the pain of malignant invasion of the skeletal tissues in various forms especially in cancer of the uterus and prostate How to help these sufferers to whom peace cannot sufficiently be brought by morphine ? Foerster in Breslau divided the posterior or sensory roots or the spinal nerves without giving much relief to patients with pain of any

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rt of the Stephen Paget lecture delivered before the Research Defence Society on Nov 4 1954 Published by courtesy of the Editor of *Conquest* the society s journal in whose January issue the lecture appears in full origin—relief, that is, commensurate with the disadvantages of denervating large areas of skin and muscle As a by-product Foerster was able to plot the nerve-supply of the different dermatomes of man in as definitive a way as is possible with something a trifle individually variable By stimulating the distal ends of the nerves he showed for the first time the vasodilatation of the vessels of the skin of the relevant spinal segment One has the feeling in reading his reports (as one had in conversation with him) that Foerster was basically an experimental physiologist rather than a therapeutist and that he chose his cases sometimes with a view to filling in a missing space in his collection of fact

A much better piece of physiology was already on the way when Foerster was doing these operations—the operation of cordotomy However Foerster had had a part in that as well, having persuaded Tietze to do and successfully, this operation

A fortunate chance fell to Spiller in Philadelphia, who observed that a coloured patient in his hospital was numb to pain and temperature up to a level on his trunk, without paralysis The sense of touch and pressure was retained This patient had tuberculosis and shortly died At the post-mortem two very small tuberculous nodules were found symmetrically placed in the spinal cord in the situation of the spinothalamic tracts There had been other suggestive evidence, notably that of Türck of Vienna, suggesting that these fibres were responsible for the transmission of pain Spiller at once saw the possibility of turning the misfortune of his patient to the good of others He persuaded a surgeon, Martin, to divide this part of the spinal cord in another person with unbearable pain The result was so great a success that the operation has since become a standard one

The optimum sites of the partial spinal sections have been worked out in recent years with great diligence by J C White of Boston, plotting the effect of limited sections of the cord under local anæsthesia No approach to the operation which is not of an experimental nature is likely to be long successful More recently still Talairach and David in Paris have tried the effects of destruction of the chief nuclei for the reception of pain in the brain itself by destroying them by electrocoagulation These are essentially human experiments of a high order and involve the use of the Horsley Clark stereotactic apparatus to which we shall shortly come back

Experimental vertical sections of the human spinal cord to relieve pain in the upper limbs were made by Donald Armour in London and Tracy Putnam in New York They have been used by the French for pelvic cancers also But these, though highly experimental in the case of man, were no more than applications of some animal experiments by Brown Séquard long ago, experiments that led Brown-Séquard to some quite wrong conclusions about sensation, since he equated "sensation" with "pain" and little else

VISCERAL PAIN

Other revelatory experiments on pain in man are those on visceral pain Such were the old observations of Lennander that crushing and burning the intestine and gall-bladder were quite painless, whereas traction on the mesentery was not John Morley investigated the agonising shoulder tip pain experienced by some patients with general peritonitis or chemical peritoneal inflammation such as follows the perforation of a gastric or duodenal ulcer He scrubbed the under surfaces of the diaphragm with gauze and abolished the referred pain by experimental procaine block of the nerves supplying the shoulder-tip area

[illegible] the same line were the experiments pursued by [illegible] others of having patients or medical students swallow inflatable bags F H Bentley and Smit using that technique, showed that the pain of duod distension was abolished by section of the spl nerves The result of important researches by se investigators was to show that distension and trac were the chief causes of visceral pain, the peri reference of which had been so acutely observed at bedside by James Mackenzie of Burnley fifty years and more cogently by Sir Thomas Lewis

No-one indeed worked with more whole heartedn in observation on the character and reference of p in human beings than Sir Thomas Lewis—the detr as it were of "clinical science," a term invented Stephen Paget's father He accepted no interpreta of symptoms that he could not experimentally verif the living subject This one sentence gives no idea the years he spent on painstaking work, and his obser tions on the pains of angina pectoris and of other visc and limb pains are classical No less were those of J Kellgren who explored the pains arising in musc fasciæ, and the ligaments of joints by injecting amounts of hypertonic saline into these structures observing the site, often at a distance, of the sev but temporary pain that followed He has told he had some 1000 painful injections of one sort or anot to find their effect Usually Kellgren was his own Lewis's test animal None of this work could have done on animals since the whole point was the descripti of the character of the pain, its situation in relation the position of the causal agent and its relation to nature of the stimulus

HEADACHE

No better example of experiment on man co found than in the investigation into the caus headache by the planned production of pain in the l Notable researches have been those of G W Pick D W C Northfield, and H G Wolff and Bronson and other collaborators, though many besides have ad their quotas

These all confirmed the ancient observation that brain itself is quite insensitive, but they added someth new It was that the stimulation of the cerebral bl vessels and some of the brain's coverings by direct indirect means led to referred pain somewhere on head's surface but according to the site of the stimulat It was shown that the violent but short-lived head that follows histamine injection is accompanied dilatation of the cerebral vessels and by a pronou increase in the amplitude of their pulsations It further shown by Pickering and Hess that their intensity of the headache corresponded with the of pulsation, being most severe when pulsation greatest

This relation between a sort of slackness of the cer vascular system and headache was confirmed by an series of observations that had results that were sur to many It was demonstrated that the surest w give a person a headache was to lower the intrac pressure by draining off cerebrospinal fluid On contrary, raising the pressure by lumbar injecti saline into a normal person, even to five times and the normal, as I have done myself, does not headache Evidently, then, the headache of a tumour or abscess or blood clot is not due to pressure alone, for some pressures experimen reached were far above those registered by most tumours

It is generally agreed that tumour headache is ca by distortion of normal intracranial relationship due either to traction on dural septa or to drag on and on the sensory cranial nerves, of which, of the trigeminal has the widest supply Some of human experiments were daring, such as those of d Wolff who introduced inflatable rubber balloons into o third and into the lateral ventricles of conscious tients and charted the sites of their induced headaches

The common headache of mankind, migraine and ondo migraine is due to dilatation of the vessels in e scalp, bone and dura mater In these cases the rebrospinal fluid pressure is never high and most lief can be obtained by the use of vasoconstrictors of e ergotamine group which it has been shown have ore effect on the extracranial arteries than on those side the dura I cannot here discuss more widely this mmonest of the pains to which mankind is heir But ough has been said to make plain how much these orkers have done to clarify a subject that was full of nfusion and of conjecture until experimental recourse as made to the right animal—man himself

### Stimulation of the Cerebral Cortex

Present-day views on epilepsy have been derived almost tirely from experiments on man The great protagonists ave been first Victor Horsley and then Ottfrid Foerster nd Krause who got only so far Much more fruitfully ave worked Wilder Penfield and Herbert Jasper and eir co-workers in the Montreal Neurological Institute

The new observations take origin not only from lectrical stimulation of the surface of the brain—even f its less exposed parts—in conscious patients but also rom direct recordings of electric potentials from the xposed brain surface in the search for damaged areas uch as could be regarded as the discharging lesions’ in Hughlings Jackson's phrase) or their synonym epileptogenic foci The discovery and excision of hese areas has led to many cures

Cortical stimulation to map out the site of the motor rea is now a commonplace of neurosurgery and has een employed by myself and by too long a list of eurosurgeons for them to be named It was early used y Victor Horsley as he reported in 1888 and again in 900 to mark out the exact piece of brain that needed moval in focal epileptic attacks or the wild involuntary ovements of a man's arm That was a straightforward iece of physiology—the application of Ferrier's work ad the much more acute observations of Sherrington hich had, to be sure, not yet seen its final fruition ith the anthropoids

More exciting were the two cases published in 1900 by arvey Cushing on sensations resulting from stimulations the post-Rolandic area in man Operating under cal anaesthesia he established the sensory function of e human postcentral strip Penfield since that day rty six years ago has greatly extended these observa ons on both the motor and sensory and other responsive eas of the brain His maps of the excitable cortex ill eventually it is to be hoped supplant those of the t and monkey so much more beloved of physiologists ecause they have been their laboratory familiars

Ferrier many years ago said that all parts of the cortex ould prove to be excitable but he could not demonstrate citability himself except from restricted areas of the ain the greater part was unresponsive Ferrier's ophecy was long unfulfilled and only recently has me closer to confirmation Thus we now know that sponses must be looked for not only in movements of *e limbs or in sensations or in flashes of light or sounds* odours but in two other directions The first is in the tonomic or visceral changes that may be the replies stimulation of some areas (changes in heart rate spiration rate blood pressure intestinal movements, c ) This work has mainly been done on animals he second and much the more exciting even dramatic scovery was made by Penfield—that stimulations of e temporal lobe in human beings may evoke experiences ctures in the mind An example may be given of the sponse of a woman of 32 who had epileptic fits of a minor sort. Each remark corresponds to a separate stimulus

> I hear singing Yes it is White Christmas
> " There is an orchestra too yes a choir That is different
> a voice—talking—a man ' Yes, I have heard it before
> a man's voice talking Yes about the same as before
> There is that sound again—like a radio programme—a man talking She said that it was a play

Results of a similar kind or the evocation of a familiar scene a moment or two only in life well accepted by the patient, in no way frightening but all with a considerable content and depth of experience have been obtained from other cases But it is by no means anybody's brain that will yield such vivid experiences confirmatory results by others must still be made Something very like that can occur spontaneously in patients with temporal lobe tumours

The upshot of this and other work is that a seizure *pattern has emerged recognisable as coming from one* or other temporal lobe It is very much to the point that these seizures, previously labelled psychomotor fits are often caused by extensive scars from damage perhaps at birth The excision of the scar and of anterior parts of the pathological temporal lobe has led to the cessation or great diminution in the frequency and severity of the attacks in a proportion claimed to be as high as 2 out of 3 cases Murray Falconer has now had some success in improving not only the fits but the behaviour of delinquent children and young adults subject to this kind of seizure Experiments carried out on man in the laudable attempt to relieve him of epilepsy has in many ways helped greatly in our interpretation of the brain's integration and of its mechanisms It marks a major advance in man's understanding of himself

The advance has been assisted by the explorations of frontal lobe physiology Our new knowledge has come about from again two sources—first major excisions of the frontal lobes of which I myself reported the first 8 European examples in 1937 and again 75 examples in 1942 Going still further Krynauw in Johannesburg reported in 1950 the first cases of removal of a cerebral hemisphere from children already hemiplegic and suffering from fits that started in the paralysed limbs It was found that the mental state of these children was often improved by the loss of half of the brain's cortex the remaining healthy half being no longer disturbed by the flow of disturbing impulses from the abnormal parts. *This was much the same conclusion as I had* reached myself from the lobectomies for brain tumour Close on the heels of that came the rising popularity of prefrontal lobotomy and its modifications for mental disorders which we owed to the inspiration of Egas Moniz (1936) All this is very much in the field of human experiment Equally experimental in their way were the introduction of the malarial treatment of general paralysis (Wagner-Jauregg 1917) and the insulin (Sakel 1927) metrazol (Meduna 1937) and electric shock therapy (Carletti and Kalinowsky 1937) of the psychoses

### Conclusion

Plainly it would be unthinkable that man should be used widely in experiment on the propagation of danger*ous infections It seems indeed that he is only suitable* as a test subject to those affections or diseases to which he alone is subject or in which his subjective responses to experiment are essential to the experiment itself This is most true of the nervous system and already his acceptance of himself in this experimental role has led to the illumination of many a dark corner I am convinced that no surgeon is quite as con cious of the truly experimental nature of his work and of the opportunities it affords for physiological observations as the neurosurgeon

# PLASMA-17-HYDROXYCORTICOSTEROIDS IN PREGNANCY

R I S BAYLISS
M.A., M.D Camb, M R C P
ASSISTANT PHYSICIAN, WESTMINSTER HOSPITAL

J C McC BROWNE
F R C S, F R C O G
PROFESSOR OF OBSTETRICS AND GYNÆCOLOGY IN THE UNIVERSITY OF LONDON

BRENDA P ROUND
B Sc Lond
RESEARCH ASSISTANT

A W STEINBECK*
M D Sydney, M R C P
LECTURER IN MEDICINE, UNIVERSITY OF QUEENSLAND

*From the Departments of Medicine and Obstetrics, Hammersmith Hospital, London*

EVIDENCE suggests that during pregnancy the activity of the adrenal cortex is increased The adrenal glands of women dying at or soon after delivery weigh more and have a larger cortex than those of non-pregnant women (*Aschoff 1910, Aschner 1912, Huggett 1950*) The urinary excretion of certain adrenocortical steroids ("glucocorticoids," "11-oxysteroids"), measured by biological and chemical methods, is increased during pregnancy (Venning 1946, Tobian 1949, Cope et al 1951) Thus, using a bio assay procedure, Venning (1946) found increased excretion of glycogenic steroids during the first trimester of pregnancy and a further increase during the subsequent months In some instances there appeared to be a reduction in the amount excreted during the last month of pregnancy, and normal values were found shortly after delivery None of the methods used gave a true estimate of the total amount of adrenocortical steroids excreted in urine, because of difficulties in hydrolysing the conjugates present (Bayliss 1952, and Hurlock 1954)

In contrast with this evidence suggesting that amounts of adrenocortical C-21 steroids are elaborat pregnancy, no increase in the excretion of androgen 17-ketosteroids has been observed by Dingemanse (1937), Hain (1939), Pearlman and Pincus (19 Venning (1946), and Jailer (1951) Although Ve (1946) found no increase in 17-ketosteroids when ured by the Pincus antimony-trichloride method, is specific for saturated 17-ketones, there was an appa increase when measured by the Zimmerman react which determines both 17-ketones and 20 ketones, latter being metabolites of progesterone, which is to be formed in increased amounts during The most complete study of the excretion of 17-k steroids in pregnancy has been made by Huis in't (1954), who found with the Zimmerman reaction the excretion of total neutral 17 ketosteroids is sli increased during pregnancy, being somewhat more the first and third trimesters than during the s Much of the increase during the third trimester was to pregnanolones and to 11-keto-etiocholanolone *11 hydroxyandrosterone—compounds believed to* metabolites of C-21 adrenocortical steroids

While the present investigation was in Gemzell (1953) reported his findings on the plasma of 17-hydroxycorticosteroids in normal pre during the last trimester the concentration was four the normal level, and very high values were immediately post partum, but the concentration returned to the normal range six days after deli No conclusion about the variation in individual resp could be drawn, because the samples of blood were from different women at different times in their nancy In the present investigation the plasma hydroxycorticosteroids were studied in the same at about monthly *intervals throughout pregnancy* during the puerperal period.

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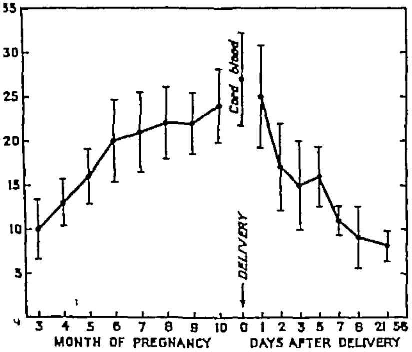
TABLE I—LEVELS OF 17-HYDROXYCORTICOSTEROIDS IN PLASMA IN PREGNANCY

| Case no | Age (yr) | No previous deliveries | 17 Hydroxycorticosteroids (µg per 100 ml) | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Months of pregnancy | | | | | | | | Cord | Days post partum | | | | | |
| | | | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | | 1 | 2 | 3 | 5 | 7 | 8 |
| 1 | 24 | 0 | | 17 | 22 | 35 | 20 | 31 | 40 | 42 | 30 | 42 | | | | | 15 |
| 2 | 24 | 1 | 4 | | 20 | 38 | 23 | 30 | 25 | | | | 37 | | | 16 | |
| 3 | 22 | 0 | | 13 | | 43 | 41 | 45 | 38 | 36 | 24 | | 23 | | | | |
| 4 | 27 | 0 | 23 | 21 | 20 | 30 | 21 | 27 | 21 | 37 | 18 | | | | | | 28 |
| 5 | 23 | 0 | | 25 | 22 | | 33 | 26 | 23 | 29 | | 37 | | | | | 2 |
| 6 | 36 | 1 | 6 | | 13 | 23 | 15 | 16 | 17 | 37 | | | 19 | | | | 9 |
| 7 | 21 | 0 | | 5 | 16 | 18 | 28 | 25 | 21 | 32 | | | | | | | 4 |
| 8 | 21 | 1 | | | | 0 | 10 | 25 | 26 | 32 | | | | | | | |
| 9 | 28 | 2 | | | | 6 | 0 | 13 | 20 | 29 | | | | | | | |
| 10 | 28 | 0 | | 8 | 17 | 24 | 28 | 30 | 22 | 30 | 50 | | | | | 10 | |
| 11 | 32 | 0 | | 11 | 5 | 9 | 30 | 20 | 31 | 16 | | | | | | | |
| 12 | 33 | 1 | | 15 | 17 | 20 | 11 | 30 | 28 | 11 | | | | | | | |
| 13 | 30 | 2 | | 7 | 5 | 19 | 33 | 18 | 16 | 23 | | | | | | | 7 |
| 14 | 29 | 1 | 4 | 11 | 12 | 15 | 12 | 13 | 22 | | | | | 27 | | | |
| 15 | 21 | 1 | 5 | 11 | 23 | 27 | 24 | 22 | | 23 | 21 | 22 | | | | 12 | |
| 16 | 33 | 1 | 8 | 13 | 26 | 14 | 18 | 23 | 27 | 26 | | | | 10 | | 7 | |
| 17 | 28 | 1 | 14 | 22 | 24 | 18 | 10 | 24 | 29 | 22 | 16 | 18 | | | 16 | | |
| 18 | 35 | 0 | | 9 | 21 | 15 | 12 | 17 | 18 | 26 | | 14 | | | 22 | | |
| 19 | 29 | 1 | 14 | 16 | 26 | 21 | | 24 | 19 | 24 | 39 | | 7 | | 9 | | |
| 20 | 27 | 1 | 8 | 11 | 15 | 28 | 22 | | 8 | 18 | | | 10 | | | | 3 |
| 21 | 28 | 2 | | | 9 | 7 | 26 | 24 | 18 | 15 | 12 | | | | | | 11 |
| 22 | 19 | 0 | | 5 | 23 | 19 | 23 | 14 | 14 | 21 | 28 | | | | | | 3 |
| 23 | 29 | 3 | | 9 | 8 | 23 | 16 | 20 | 22 | 12 | | | | | | | |
| 24 | 20 | 0 | 17 | 21 | 10 | 11 | | 16 | | 23 | 30 | 17 | | | | | |
| 25 | 27 | 0 | 21 | 15 | 17 | 18 | 10 | 13 | 26 | 20 | 40 | | 22 | | | | 14 |
| 26 | 33 | 3 | | | 13 | 21 | | 21 | 21 | 16 | | | | | | | 7 |
| 27 | 17 | 0 | 8 | 16 | 15 | 21 | | 13 | 18 | 19 | 29 | | | 9 | | 10 | |
| 28 | 30 | 1 | 3 | 11 | 16 | 18 | 19 | 19 | 20 | 15 | 22 | | 9 | | | | |
| 29 | 29 | 1 | | | 5 | 3 | | 18 | 16 | 12 | 17 | | | | | | 4 |
| 30 | 24 | 1 | | 14 | 13 | 15 | | 11 | 15 | 18 | 21 | | 12 | | | | 8 |
| Mean | | | 10 | 13 | 16 | 20 | 21 | 22 | 22 | 24 | 27 | 25 | 17 | 15 | 16 | 11 | 9 |
| Standard error of m | | | 1 9 | 1 1 | 1 2 | 1 7 | 1 8 | 1 5 | 1 3 | 1 6 | 2 7 | 4 8 | 3 6 | 5 8 | 3 8 | 1 5 | 2·0 |



—Mean level (and standard deviation) of 17-hydroxycorticosteroids plasma at each month of pregnancy and during puerperium in lthy women.

## Material and Methods

lirty eight women attending the antenatal clinic for first time in their present pregnancy were chosen at lom Eight subsequently developed complications iding toxæmia anæmia and hypertension, and have excluded from this report Of the remaining thirty underwent a normal pregnancy twenty nine were rered spontaneously and one had a cæsarean section use of a contracted pelvis Eighteen had borne lren before (table I)

imples of blood were taken at the first attendance thereafter at monthly intervals all these ante um samples being collected at about the same time ne afternoon In fifteen instances blood was collected n the umbilical cord at the time of delivery and further ples were taken from the mothers at various intervals eafter

he concentration of 17 hydroxycorticosteroids in the ma was estimated by a modification of the method Nelson and Samuels (1952) described by Bayliss and nbeck (1953) Compounds measured by this technique ude cortisone, cortisol (hydrocortisone) and their dro and tetrahydro metabolic reduction products mean plasma value for healthy women is 9 5 µg 100 ml with 95% fiducial limits of 3–16 µg per 100 ml

## Results

he results are shown in table I the month of pregnancy ng calculated from the time of delivery and the mean ls of 17 hydroxycorticosteroids in the plasma of the ty women at each month of pregnancy are shown in 1 At the third month the level of 10 µg per 100 ml he same as the mean value for non pregnant women reafter the level rises steadily the highest level ched being 24 µg per 100 ml during the last month gestation At the time of delivery the level in the bilical-cord blood was slightly higher than during the month of pregnancy Post partum the level in the ternal blood was high for twenty four hours and then urned gradually to a normal level by the eighth

The individual patients however showed considerable ation from the mean values In all of them the level 17 hydroxycorticosteroids in the plasma rose but in ne (cases 1–13) it rose higher than 20 µg per 100 ml some time during pregnancy, whereas in others ses 14–25) it rose to only 21–28 µg per 100 ml. and three (cases 28–30) it did not exceed 20 µg per 100 ml strative examples from each of these three arbitrary ups are shown in fig 2 No clinical differences were noted between the patients with the high and with the lower levels

In most instances the levels during the third and fourth months were within the normal range for non pregnant women, but high values were found in some at this time About half the patients had abnormally high levels by the fifth month and others, although not having abnormally high levels showed an increase above the values observed during the previous two months During the last month of pregnancy there was in most instances a further increase or no significant change compared with the levels in the eighth and ninth months, but in seven patients a definite fall took place at this time (cases 3 11 12 21 23 28 and 29)

Although the mean values for the cord blood and mother s blood in the last month of pregnancy were not significantly different in eight cases the cord blood had a higher level in five a lower and in two there was no significant difference

During the postpartum period there were considerable individual differences in the plasma steroid levels. Most of the patients had abnormally high values for the first forty eight hours after delivery Two had raised levels after this time one (case 14) on the third day and the other (case 18) on the fifth day Case 4 who had unusually high levels at the third month of pregnancy, also had a high level on the eighth postpartum day she was particularly anxious, and the high levels may have been related to emotional disturbances

No correlation was found between the height of the 17 hydroxycorticosteroid level during pregnancy and the weight of the placenta or of the baby at birth

## Discussion

These results show that in pregnancy the level of 17 hydroxycorticosteroids in the plasma is raised, in some cases to levels exceeding those found in patients with Cushing s syndrome (Perkoff et al. 1954 Bayliss and Steinbeck unpublished)

At least two problems remain unanswered what is the nature of the material which is present in increased amounts, and what is its origin ?

### *Nature of Material*

The chemical method used for the estimation of 17 hydroxycorticosteroids is relatively specific for 17 : 21 dihydroxy 20-ketosteroids such as cortisone cortisol and their dihydro- and tetrahydro derivatives We have found that in healthy non pregnant women the plasma

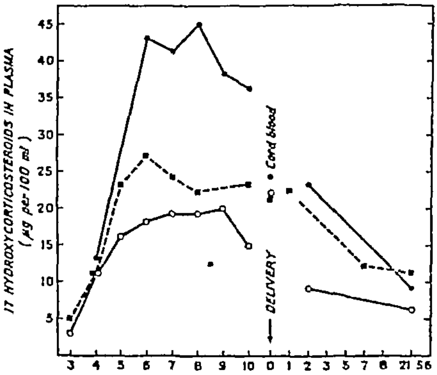


Fig 2—Three examples of the individual variation of 17-hydroxycorticosteroids in plasma during pregnancy

17-hydroxycorticosteroid levels are a measure of the amount of cortisol and also more polar derivatives—e g , tetrahydrocortisone Without further chemical analysis it is impossible to say what is the exact nature of the material measured in the plasma of pregnant women, but by paper chromatography Bush (1953) has found increased amounts of cortisol in the blood of such patients

*Origin of Increased 17-Hydroxycorticosteroids*

If the site of origin were either the fœtus or the placenta, the steroid levels in the mother would be expected to fall more rapidly after delivery than they do For example, after a single dose of cortisol acetate 200 mg by mouth the plasma level of 17-hydroxycorticosteroids falls from a maximum of more than 100 µg per 100 ml to normal levels within eight hours (Nelson et al 1952) In newborn infants the urinary excretion of 17 ketosteroids, glycogenic corticoids, and reducing steroids, and the plasma level of 17-hydroxycorticosteroids are low (Talbot et al 1943, Day 1948, Venning et al 1949, Klein et al 1954) Since Klein et al (1954) have found low 17-hydroxycorticosteroid levels in the blood of newborn infants but, like us, high levels in most samples of umbilical cord blood, it seems reasonable to deduce that the high level in the cord blood results from the high concentration in the maternal circulation, and that the hormones pass readily across the placental barrier Although small amounts of adrenocortical hormones have been found in placental extracts, it is impossible to tell whether these were produced in the placenta or are present in the blood retained there (Johnson and Haines 1952, de Courcy et al 1952) That some adrenocortical like steroid material is formed in the placenta is suggested by observations made on patients with Addison's disease who have become pregnant The excretion of 17-ketosteroids in two women with this disease has been studied during three pregnancies by Samuels et al (1943), Knowlton et al (1949), and Jailer and Knowlton (1950) In all three instances the amount excreted increased and in the last trimester reached normal levels In one patient the 17-ketosteroids were estimated by the Zimmerman reaction, and in the other by the same method during the first pregnancy and by the antimony-trichloride reaction in the second During the later part of the second pregnancy increased amounts of neutral reducing lipids were found in the urine and after delivery the excretion returned to abnormally low addisonian levels

TABLE II—LEVELS OF 17 HYDROXYCORTICOSTEROIDS IN PLASMA AT CÆSAREAN SECTION

| Case no | 17 Hydroxycorticosteroids (µg per 100 ml ) | |
|---|---|---|
| | Antecubital vein | Placental sinus and uterine blood |
| 31 | 55 | 45 |
| 32 | 46 | 48 |
| 33 | 35 | 19 |
| 34 | 50 | 42<br>42* |

* Specimen obtained from an anterior uterine vein before uterus was opened

Further evidence about whether the material is formed in the maternal adrenal glands or the placenta was sought by taking samples of blood simultaneously at cæsarean section from an antecubital vein and a placental sinus The results, shown in table II, are inconclusive because the steroid level was much the same in samples from both sites, and significantly the level in placental sinus blood was not higher than in the general circulation

It seems probable that the main site of origin of the 17 hydroxycorticosteroid material in pregnancy is the maternal adrenal glands because the glands are hypertrophied and during the puerperium the steroid level falls gradually The corticotrophic hormone responsible this increased adrenal activity could come from eith maternal pituitary or the placenta, which is known produce trophic hormones such as gonadotrophins, there is some experimental evidence that a hormone corticotrophic like activity can be extracted from placenta (Jailer and Knowlton 1950, Opsahl and L 1951, Tarantino 1951, Cohen and Kleinberg 195

Increased formation of 17 hydroxycorticostero pregnancy may explain why some patients with rh toid arthritis have a clinical remission at this time why diabetics may require increased amounts of in during pregnancy

## Summary

The plasma level of 17-hydroxycorticosteroids has b followed at about monthly intervals through the nor pregnancy of thirty women At delivery samples blood were taken from the umbilical cord, and therea from the mother at various intervals in the postpa period

The level of 17-hydroxycorticosteroids in the pl rose progressively during pregnancy, becoming in s patients very high After delivery the level fell, re to normal after a week

The nature and origin of the material formed pregnancy are discussed

We are grateful to Miss J Pirkis for her constant cons tious technical assistance, and to the nurses of the antena clinic and obstetric wards for their coöperation *This* w was supported in part by a Lund grant from the *Dia* Association

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" It is a strange reflection that compels us to a that while food, water and milk supplies are carefully su vised and protected in order to guard the alimentary tract members of the general public, state and local legislation but little interest in the protection of the very delicate sensitive membranes lining the respiratory tracts of the general public "—W S WALTON, M D , medical officer health for Newcastle upon Tyne, in his report for 1953, p

# TUBERCULOUS MENINGITIS TREATED WITH CORTISONE

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IN tuberculous meningitis exudate may cause vascular clusions and fibrosis leading to cranial nerve palsies, yelitis hydrocephalus and spinal block Any manœuvre welcome which lessens the incidence of these complica ons and shortens the stay in hospital

Hitherto efforts to combat local obstruction produced y tuberculous exudate have been restricted to the troduction of purified protein derivative of tuberculin eparin streptokinase, and even trypsin into the cerebro oinal fluid (C S F ) after the obstruction has developed uch measures have in the main been hazardous and isappointing in their results

To prevent the formation of tuberculous exudate eemed more rational than to try and remove it after had been formed Because of its known property of iscouraging local tissue reaction we tried cortisone om the very beginning of treatment adding it to our stablished routine of intramuscular and intrathecal reptomycin and oral isoniazid Although alive to the heoretical dangers of giving cortisone to patients with uberculosis we were further encouraged to take this tep when we became aware of the fact that isoniazid, dmittedly a highly effective antituberculous agent seemed to cause tuberculous lesions to become initially nore vascular and swollen (Ritchie et al 1953 Dick 954) than either *p* aminosalicylic acid (P A S ) or strepto mycin This fact though not of great importance in ulmonary or renal tuberculosis, could be responsible or precipitating hydrocephalus or spinal block in patients vith tuberculous meningitis The simultaneous adminis ration of cortisone with the antibiotics might minimise hese changes in the tuberculous lesions and thus prevent bstructions

## Material

This report concerns twelve patients all adults with uberculous meningitis who were treated in the neuro ogical unit of the Whittington Hospital All were given ntramuscular and intrathecal streptomycin together with oral isoniazid, half of them were also given cortisone rom the beginning of treatment. Although not formally ontrolled the group receiving cortisone is comparable with that treated conservatively These numbers are oo small and the follow up period is too short for efinite conclusions to be drawn but the results are suffi iently encouraging to justify a preliminary publication.

## Method

Our routine was to give intramuscular streptomycin 1 g and oral isoniazid 400 mg daily *for six months, and* ntrathecal streptomycin 50 mg daily for from three to ive months No single criterion such as the C.S F ugar level is an adequate guide to when it is safe to stop he intrathecal streptomycin We have taken the patient s eneral condition shown by his weight temperature and rythrocyte sedimentation rate (E.S R.) together with he C.S F findings (rising level of sugar—preferably bove 40 mg per 100 ml —and falling cell-count) nto consideration We stopped giving intrathecal treptomycin when all these factors had been favourable or a month This routine was unnecessarily conservative Shane and Riley 1953 Lorber 1954), but all twelve atients were judged by the same standards

## Results

### Standard Treatment

The first six consecutive cases in this series were given the standard treatment Two were classified as early cases (Medical Research Council 1948) and four as intermediate

CASE 1 had a left hemiparesis on admission her physical signs were unaltered when she was discharged

CASE 2 developed bilateral optic atrophy becoming blind only after she had clinically recovered from the meningitis.

CASE 3 developed spinal block and blindness, went steadily downhill and died in three months At necropsy a great deal of thick exudate was found round the spinal cord and the base of the brain. His infecting organism was fully sensitive to streptomycin isoniazid and P A.S in vitro He was given some cortisone but only after the development of his complications when he was moribund

CASE 4 developed no neurological sequelæ but during the course of her miliary and meningeal tuberculosis she had severe hypoplasia of her bone-marrow with anæmia and leucopenia necessitating frequent blood transfusions. Her spleen was enlarged and soft at this time Under treatment her blood picture gradually became normal and her spleen impalpable but some months after her discharge from hos pital she developed hypersplenic pancytopenia her bone marrow was hyperplastic her spleen enlarged and firm and her peripheral blood poor in all the formed elements Splenectomy was followed by complete remission

CASE 5 developed a spinal block and required daily cisternal puncture for six months during the third month she became deaf

CASE 6 recovered uneventfully

### Standard Treatment plus Cortisone

The next six patients to be admitted were given corti sone from the outset in addition to the usual antibiotic therapy Cortisone was given to them as follows: 300 mg in divided doses on the first day 200 mg on the second and 100 mg on the third and every subsequent day until the intrathecal streptomycin was stopped To prevent suprarenal exhaustion the cortisone was then tailed off and covered by a short course of corticotrophin for twelve days thus

First three days cortisone 25 mg and corticotrophin 10 units

Second three days cortisone 12 5 mg and corticotrophin 20 units

Third three days corticotrophin 20 units but no cortisone

Fourth three days corticotrophin 10 units but no cortisone

All the patients on cortisone were given potassium chloride 3 g daily by mouth Serum-electrolytes were examined weekly

Of this second group of six cases one was classified as early and five as intermediate

CASE 7 had a left sixth nerve palsy and extensor plantar responses on admission

CASE 9 was stuporose and incontinent and had extensor plantar responses

CASE 10 had cerebellar signs and extensor plantar responses as did CASE 11 and CASE 12 both of whom were very dis oriented All these patients made rapid and uneventful recoveries as did case 8

CASE 8.—In addition to miliary tuberculosis and tuber culous meningitis this patient had several enlarged glands in his neck. These were thought to be tuberculous but were not considered to be a contra indication to the use of cortisone A month after the onset of treatment the glands broke down and had to be curetted The patient felt remarkably well throughout this and his meningitis cleared up without complication

## Discussion

As Brooks et al (1954) observe in tuberculous meningitis antibiotics have only a restricted effect if the circulation of the C.S F is interfered with as in spinal block They conclude that an agent must be found which can rapidly disperse fibrin and they say

> It is also clear that early prophylactic use of such an agent would be more effective than its therapeutic use under conditions of established or incipient block

Though there is no evidence that cortisone has any effect on fibrous tissue it is known to inhibit the formation of exudate It therefore seems essential to give it as soon as possible after tuberculous meningitis has been diagnosed Not only is it necessary to prevent the mechanical obstruction caused by the exudate, but the associated endarteritis and neurological damage resulting from it are unlikely to be reversible except in their earliest stages

Houghton (1954) has shown that prolonged courses of corticotrophin can be safely given to tuberculous patients while they are on full antibiotic treatment, his patients had pulmonary tuberculosis and were given corticotrophin for drug sensitivity He observed that corticotrophin not only dealt with the allergic manifestations but also "revolutionised" the patient's morale Jahn et al (1954) describe the use of corticotrophin and cortisone with antibiotics in the management of overwhelming infections such as peritonitis, meningococcal meningitis, and lobar pneumonia

Several reports have now been published abroad describing the use of cortisone or of corticotrophin in tuberculous meningitis Shane and Riley (1953) reported eight cases treated with cortisone in addition to the usual antibiotics (five of these were not treated with intrathecal streptomycin) These workers thought the cortisone had a beneficial effect on the course of the meningitis Bulkeley (1953) described the use of corticotrophin in thirty one cases of tuberculous meningitis in children Although it is not clear from the analysis that corticotrophin and not isoniazid was responsible for the improved mortality-rate in that series, at least it is evident that corticotrophin can be given to such patients without mishap Wasz Höckert (1954) has used cortisone and intrathecal hydrocortisone in the treatment of tuberculous meningitis in Helsinki, it is described as "routine" treatment in his unit now de Lavergne et al (1954) report its use in eighteen patients with tuberculous meningitis

Our two groups of patients can conveniently be compared under three headings the patient's general condition, the changes in the C S F, and the neurological complications All the patients who were given cortisone showed a very striking and early clinical improvement Whereas those treated conventionally (the first six patients) remained confused, uncooperative, and miserable for a week or ten days after beginning treatment, those who were given cortisone at the start were fully oriented, alert, and cheerful within two or three days The E S R of the cortisone-treated patients fell noticeably sooner, though this may have been a non-specific effect of the hormone Their appetites improved earlier than those of the controls, they gained weight more rapidly, and they clamoured to be allowed to get up within a week or two

The C S.F findings differed in the two groups, in particular the cell count fell very much more rapidly in the patients on cortisone than in the controls This was not unexpected, since cortisone was given largely to prevent a severe cellular response in the meninges At the same time, in some of the patients on cortisone the C S.F sugar level rose to normal very early, this also may have been a non specific effect of the hormone and might not necessarily indicate recession of the tuberculosis

There was a striking difference between the two groups in the incidence of neurological complications Of the controls one died and three have permanent stigmata, whereas all those treated with cortisone recovered completely without complications

The prolonged administration of cortisone may be attended by retention of salt and depletion of potassium Clinical evidence of this may be anticipated by the weekly estimation of serum electrolytes All patients treated with cortisone should be given additional potassium chloride by mouth The catastrophe of suprarenal failure may be avoided by covering the withdrawal of c[illegible]e by a short course of corticotrophin The danger of lighting up an old infection, such as osteomyel is real, and careful inquiry should be made into patient's previous illnesses Every precaution must taken to protect a patient on cortisone from acq secondary infection, since he may be unable to loca it adequately, and septicæmia may result

The danger of disseminating tuberculosis throu the body may be advanced as a contra indicatio cortisone therapy in tuberculous meningitis How many patients with this disease also have miliary t culosis, in them the process could hardly be disseminated Indeed, with effective antibiotics c sone therapy may accelerate recovery by rendering tubercle bacillus more accessible, it is less likely become walled off inside caseous material surround by a fibrous wall and with a poor blood-supply In patient with tuberculosis or any other infection trea with cortisone the appropriate antibiotics must continued after withdrawal of the hormone

Although it is not strictly relevant to the issue treating tuberculous meningitis with cortisone, we that mention must be made of the present trend withholding intrathecal streptomycin from select cases Some cases of tuberculous meningitis can d be "cured" without intrathecal streptomycin, provi that they are treated with full doses of oral and intramuscular streptomycin Early cases are in which there is the greatest incentive for withh intrathecal therapy It is not by any means esta that this is safe in all cases, however, and most treating tuberculous meningitis are giving intrathe streptomycin for at least four to six weeks Wh course is adopted, we believe that there is enough ev to show that the addition of cortisone to the trea of tuberculous meningitis has important advanta and merits further trial in a larger controlled series

## Summary

In this report six consecutive cases of tub meningitis treated by routine methods are comp with the next six patients admitted with this disea who were treated in the same way except that corti was added

Neurological complications occurred in four of t six control patients, and one of these died The patie treated with cortisone all recovered completely, with any neurological complications, and their clinical impro ment was much more rapid than that of the controls*

No complications of cortisone therapy were

Cortisone must be given from the beginning of t ment and with full antibiotic cover, which should conti for several weeks after the cortisone has been withdra

A more extensive clinical trial should be underta into the value of cortisone in the treatment of tubercul meningitis

We wish to thank the workers at the Whittington Gr Laboratory for their coöperation, Dr Arnold Bloom for advice about two of our patients, and Miss E M Mar for help with the foreign references

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* Since the preparation of this report the last case (12) of the has developed spinal block and impairment of vision althou is otherwise well Only much greater experience of the complications could show whether cortisone reduces th incidence or could avert them if continued for a longer per

# KIN REACTIONS BENEATH ADHESIVE PLASTERS

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LTHOUGH medical and surgical plasters have been d for many years comparatively few clinical investi ions have been undertaken into the skin reactions eloping beneath them

eck et al (1948) described three types of reaction duced by adhesive tape (1) a fleeting reaction cting mostly hairy areas due to the mechanical uma of removing the tape (2) a specific sensitivity to or more ingredients of the plaster and (3) a reaction to change in pH and to the growth of bacteria on the beneath the plaster

Humphries (1947) has shown that moulds and bacteria w beneath ordinary adhesive plasters By adding salts of propionic acid and of caprylic acid to ordinary ster he found that of 130 patients who reacted to the ginal plaster only 5 reacted to the enhanced one reased tackiness was also noted after the plaster had n in position for seven days this might be due either the added fatty acids or to the decrease of maceration sequent on the reduction of bacterial flora beneath the ster Gaul and Underwood (1949) were unable to stantiate the observation that the incorporation of tericidal substances in the adhesive mass tended to rease the incidence of adhesive-tape dermatitis

eck et al (1948) found that the pH of normal skin was the pH increased to 6 3 after seven days and to after fourteen days beneath ordinary plaster but only 5 7 after seven days and to 6 4 after fourteen days eath plaster to which fatty acids had been added e bacterial flora decreased beneath both plasters but ecially beneath the one containing fatty acids

We consider that at least five types of reaction may elop beneath adhesive plasters owing to the following ises

1) Trauma of removal
2) Irritation by the adhesive
3) Retention of sweat and serous discharges on the skin ding to maceration of the horny layer
4) Favourable or unfavourable disturbance of the bacterial a by selective antibacterial action of some constituent the spread
5) Eczematous sensitisation to some substance in the esive spread or in the rubber

## Trauma of Removal

The traumatic reaction of removal occurs mostly at sebaceous orifices and is manifested as follicular ules with some diffuse or blotchy erythema It is atest with very tacky plasters and becomes milder if plaster has remained in situ for more than five days e reaction develops a minute or two after removal of plaster particularly at hairy sites and if a plaster vent has not been used to assist removal It has to be ferentiated from the reaction of irritation which elops only after a plaster has been in situ for some ee to five days and is then seen immediately the ster is removed Although Glick et al (1948) have ommended propylene glycol ethyl ether as a non gic and non inflammable remover of adhesive plaster have found that ether is entirely satisfactory for this pose provided the danger of its inflammability is preciated

## Irritation from Adhesive

rritation effects show as red papules and pustules, netimes with moist pink areas but without vesiculation e reaction is due to mechanical stimulation of the mation of keratin by the adhesiveness of the spread or by some chemical constituent of the adhesive mass There is also interference with desquamation The sweat-ducts are obstructed at their orifices along the epidermal ridges, and there is a milder hyperkeratosis and plugging of the ostia of the pilosebaceous follicles This reaction is more pronounced in sweaty people and in hot humid surroundings It appears clinically five days or more after the plaster has been applied but Peck et al (1951) observed histological changes within three days of the application of a plaster Any pre existing acne at the site of application of the plaster may be aggravated within forty eight hours giving a papular or papulopustular reaction (fig 1D)

Rubin (1949) showed that hyperkeratosis could be produced by slight continuous mechanical irritation —e g from the small range of movement of adhesive tape over the skin Another factor may well be the kerato plastic properties of certain chemicals particularly coal tar derivatives Thus chlorinated phenols are known to stimulate the formation of keratin and in this category is chloroxylenol which is contained in liquor chloroxylenolis *B.P* (roxenol) and in Dettol 'Germosan Neo monsol 'Osyl Streph Zant and several other proprietary antiseptics This substance has in the past been incorporated in plasters by some manufacturers

Infection often develops in the ducts and follicles beneath the ostial obstructions either mild when it is due to *Staphylococcus saprophyticus* and other sapro phytes or frankly purulent when it is due to *Staph pyogenes Pseudomonas pyocyanea* or *Proteus vulgaris* The process is analogous to that of miliaria rubra ( prickly heat )

We have tried to discover if there is any quantitative relationship between the adhesiveness of a plaster and its irritating effects on the skin For this purpose plaster discs of three known degrees of adhesiveness were applied to the backs of 31 students in random fashion over the scapular regions, and the number of papules beneath each disc was counted after it had been in position for a week If part of a patch became detached, the fraction of adhering remainder was estimated and the papule count was adjusted to what it would have been if the whole patch had remained in contact with the skin The results are summarised as follows :

| *Adhesiveness (G per sq inch)* | *Average no of papules per 0 6 sq cm* |
|---|---|
| 705 ± 65 | 14 7 |
| 445 ± 40 | 12 3 |
| [illegible]00 ± 80 | 11 1 |

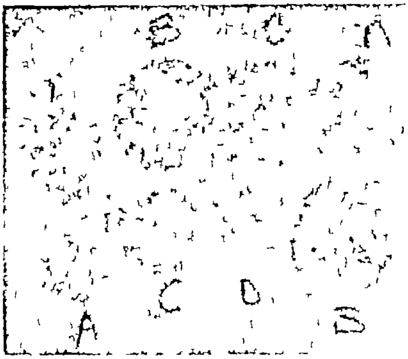


Fig 1—Patch-tests made with : A, standard plaster ; B plaster without chloroxylenol ; C, standard plaster ; D plaster made with deproteinised rubber Note positive eczematous response to A B and C, and effect of irritation alone of D probably due to coincident acne vulgaris.

The figures (which are not recorded here) have been considered statistically by Mr E C Fieller, who has expressed the view that they show quite conclusively the liability of the number of papules to increase with the adhesive strength of the plaster This does not exclude the probability that plasters of equal adhesive strength may vary in their tendencies to irritate by virtue of other differences in their physicochemical properties, and we hope to study this problem further when suitable plasters of equal adhesiveness but of different composition can be provided

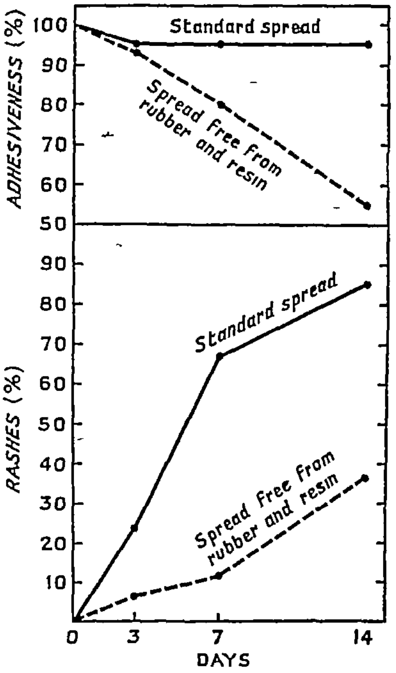


Fig 2—Incidence of rashes according to adhesiveness of plaster

Fig 2 compares the incidence of rashes when very adhesive plasters and less adhesive plasters are applied The plasters used were (1) a porous plaster of standard spread, and (2) a porous plaster said to contain neither rubber nor resin It will be observed that there were far fewer rashes from the latter plaster (37%) than from the former (85%), but its adhesion at the end of fourteen days was only 55% against 95% with the standard spread We have already indicated that the reaction of irritation depends inter alia on adhesiveness The plaster with only 55% adhesion is effective as a bandage wound round a limb but relatively ineffective for small patch dressings, and it should be called "semi adhesive" to differentiate it from "fully" (or 95%) adhesive plasters

We found that waterproof and ordinary plaster approximately similar adhesiveness produced much same number of papules, suggesting that the opera factor is the physicochemical properties of the pl constituents and not the degree of permeability of t backing material

One patient (case 25 in table) gave strongly pos reactions to the plaster mass, all constituents, ben and distilled water He had dermographia, and r developed at all sites It was considered that this wa example, not of contact eczematous dermatitis, but dermographia caused by the trauma of removing patches

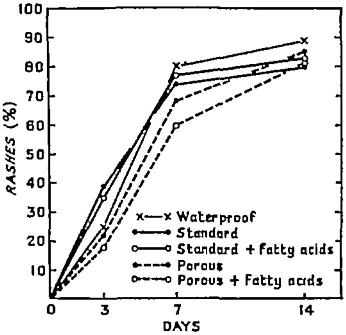
### Retention of Sweat and Discharges

Retention of sweat and serous discharges may l to maceration of the horny layer, infection, or infec eczema Peck et al (1951) found that a propion caprylate fatty-acid solution applied to the skin be the application of plasters diminished the incidence erythema, œdema, and oozing but not the number papular reactions At the same time, the bacterial f was noted to be progressively reduced according to number of applications of the fatty acid solution have made patch-tests on 35 students with porous non porous adhesive plasters, with and without 0 zinc propionate and 0 6% zinc caprylate incorpora Plasters with fatty acid added produced a slightly r incidence of rashes (with the porous plasters but with the non porous ones) (fig 3) The incider rashes was slightly less with porous than with non adhesive spreads up to seven days but not sub A waterproof plaster produced the highest incidence rashes after a week, but the difference betwee curves was so slight as perhaps to be insignifica "Porous" bandages are only partially porous, th leave uncovered only a small proportion of the sw ducts and sebaceous follicles They have the degree of impermeability between perforations as l similar non porous bandages all over their surface certain circumstances the perforations may be obstructed after a few days by detritus or disch Nevertheless Scheffler and Lindner (1952), in a stu 100 patients, found that porous plasters were tolerate best E M Bavin (personal communication) has that the permeability of non-porous plasters to vapour is 100 G per sq metre per twenty four h and of porous plasters 3500 G per sq metre per t

REACTIONS

| Reactions to | Case no | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 2 |
| Plasters | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | +* | + | + | |
| Roxenol | | | | + | + | − | | | − | + | ± | − | − | + | − | | | | + | − | | − | ± | |
| Fully adhesive plasters | 3/3 | 3/3 | 1/1 | 1/1 | 1/1 | 4/1 | 3/3 | 2/2 | 3/3 | 9/2 | 1/1 | 1/1 | 1/1 | 1/1 | 3/2 | 5/3 | 5/5 | 1/2 | 1/1 | 1/1 | 0/1 | 1/1 | 1/1 | 5 |
| *Components in arachis oil* | | | | | | | | | | | | | | | | | | | | | | | | |
| Arachis oil | − | − | − | − | − | − | − | − | − | − | | | | | | | | | | | | | | |
| Flectol H | − | − | − | − | − | − | − | − | − | − | | | | | | | | | | | | | | |
| Chloroxylenol | − | − | − | − | − | − | − | − | − | − | | | | | | | | | | | | | | |
| Crêpe rubber | − | − | − | − | − | − | − | − | − | − | | | | | | | | | | | | | | |
| Smoked rubber | − | − | − | − | − | − | − | − | − | − | | | | | | | | | | | | | | |
| Colophony | − | − | − | − | − | − | + | − | − | − | | | | | | | | | | | | | | |
| *Components in benzene* | | | | | | | | | | | | | | | | | | | | | | | | |
| Benzene | | | | − | − | − | − | | − | − | − | − | − | − | − | − | − | − | − | ±† | − | ‡ | | |
| Flectol H | | | | − | − | − | − | | − | − | − | − | − | − | − | − | − | − | − | ± | − | ‡ | | |
| Chloroxylenol | | | | + | + | − | − | | − | + | − | − | − | + | − | − | − | ± | − | + | − | ‡ | | |
| Crêpe rubber | | | | − | − | − | − | | − | − | − | − | − | − | − | − | − | + | − | − | ± | ‡ | | |
| Smoked rubber | | | | ± | − | − | − | | − | − | ± | + | − | − | − | − | − | + | ± | ± | − | ‡ | | |
| Colophony | | | | − | − | + | + | | + | ± | − | − | − | − | − | + | − | − | − | + | − | ‡ | | |
| Mixed components | | | | | | + | + | | − | − | | | − | | | | − | | | | | | | |
| *Elimination tests* | | | | | | | | | | | | | | | | | | | | | | | | |
| Plaster without chloroxylenol | | | | | | | | + | + | + | + | ∓ | + | + | | | | | + | + | | ± | ∓ | |
| Plaster without rubber proteins | | | | | | | | − | + | + | − | − | − | + | ± | | | ± | ± | ± | − | − | | |
| *Conclusions* | | | | | | | | | | | | | | | | | | | | | | | | |
| Sensitivity | U | U | U | P | P | C | C | R | C | P+C | R | R | RC | PIM | IRC | C | U | RIP | IR | IU | IIR | R | P | |

* er 5 days † read at 5 days ‡ patches fell off § dermographia C colophony I irritation effects ID irritat mographia M, multiple P, chloroxylenol R, rubber RC rubber protein complex in plaster mass U, undetermin



g 1—Incidence of rashes according to composition of plaster

hours The permeability is estimated by measuring ;ain in weight of a Polythene canister filled with um chloride, which has a lid with a circular hole ı in diameter covered with the adhesive tape being d The canister is kept under standard conditions )°C temperature and 90° relative humidity and is hed at regular intervals

### Disturbance of Bacterial Flora

ıe bacterial flora may be disturbed when manufac 's incorporate an antiseptic—e.g , chloroxylenol—in adhesive spread Chloroxylenol is a potent bac ide against *Streptococcus hæmolyticus* but much less 'e against *Staph pyogenes* and almost inactive against *ɔyocyanea* and *Proteus vulgaris* (*Extra Pharmacopœia* ) This disparity of action against different organisms predispose to staphylococcal proteus or pyocyanea :tion ( ecological drug eruption) or to the pro ion of a bacterial eczema perhaps with secondary spread "autolytic" eczema

### Eczematous Sensitisation

ɔntact eczematous reactions to some chemical con ıent of the adhesive spread or of the rubber are h rarer than reactions caused by irritation They ılop after a latent period of days on the first exposure, fter a few hours with subsequent exposures, and are ıcterised by erythema œdema, and vesiculation constituents of plasters which are most likely to be onsible include colophony resin (rosin) crêpe rubber ked rubber rubber antioxidants plasticisers and septics which some makers have thought it wise to rporate Of the other constituents wool fat (lanolin) nown to be a very occasional sensitiser in 1 14% of ımatous people but much less than this in the general ulation (Sulzberger et al 1953) Liquid paraffin zinc oxide are unlikely to upset the skin

ı trying to find the commoner causes of contact-matous reactions from adhesive plaster we applied individual constituents dissolved in arachis oil on ll squares of gauze held in place by an adhesive of irritative and sensitisation potential to people known ɔo sensitive to the plaster mass Negative results ı obtained in 9 of 10 cases the exception being a tive reaction to colophony Further trials were then o with the constituents dissolved in benzene and tive results were obtained in most of the patients ɔd

ho substances were made up into solutions containing ·1 ml the amount of each constituent present in ı cm of the composite plaster The results were rved at forty eight hours and once more at to seven days The substances tested were as :lws

(1) Benzene (control)
(2) 0 1% Flectol H a plasticiser and antioxidant
(3) 0 25% chloroxylenol
(4) 5% crêpe rubber containing no antioxidant
(5) 5% smoked rubber containing very little antioxidant, probably of hydroquinone type and some oxidation products of the smoking process
(6) 5% colophony resin, the chief constituent of which is abietic acid said by Schwartz et al. (1947) to be an irritant to hypersensitive people

The results were as follows

| | |
|---|---|
| Number of patients tested to constituents in benzene | 10 |
| Positive to 5 0% colophony | 4 |
| Positive to 0 25% chloroxylenol | 3 |
| Positive (?) to 5·0% crêpe rubber | 1 |
| Positive to 5·0% smoked rubber (2 ? positive) | 3 |
| Positive to 0 1% flectol H | 0 |
| Positive to benzene | 0 |
| Positive to colophony and to chloroxylenol | 1 |
| Positive to crêpe rubber to smoked rubber and ? to chloroxylenol | 1 |
| Positive to multiple factors (probably irritant effect) | 1 |
| Positive to every patch (due to dermographia) | 1 |
| Negative to all constituents | 3 |
| Invalid (patches fell off after a few hours) | 1 |

Trials have been made with deproteinised rubber plasters and with chloroxylenol free plasters on suitable patients People sensitive to chloroxylenol tolerate a plaster free from this substance, and people sensitive to either crêpe or sheet rubber are tolerant of adhesive dressings made with deproteinised rubber (fig 1) On the other hand, people sensitised to colophony have continued to react to plasters free from chloroxylenol or from protein fractions of rubber The results were as follows

| | |
|---|---|
| Positive to plaster with chloroxylenol and negative to plaster without chloroxylenol | 2 |
| Positive to plaster with rubber proteins and negative to plaster without rubber proteins | 5 |
| Positive to plaster with rubber proteins and doubtful to plaster without rubber proteins | 4 |
| Positive to plasters with and without chloroxylenol and with and without rubber proteins | 3 |

(Rubber is deproteinised by a complex process of ammoniation and centrifugation which throws out the proteins salts and possibly the natural antioxidants Treatment with trypsin hydrolyses any remaining protein after which further centrifugation is done followed by coagulation with acetic acid )

From these tests the following conclusions were drawn :

| | |
|---|---|
| Sensitive to chloroxylenol | 6 (1 7) |
| Sensitive to colophony | 5 |
| Sensitive to rubber | 5 (1 7) |
| Sensitive to rubber-adhesive complex | 1 (1 2) |
| Multiple sensitivity | (1 1) |
| Irritation effects | 4 |
| Irritation effects through dermographia | 1 |
| Undetermined causes (of which 3 were tested to ingredients in arachis oil and 1 was tested to ingredients in benzene in the 5th the effects were probably due to irritation) | 5 |

For the detailed results see the accompanying table

The foregoing clinical results are supported by the results of experiments on animals made in the laboratories of Smith & Nephew Research Ltd by Mr E M Bavin B.SC., and Miss B James B SC to whom we are indebted for the following summary of their work

> Our technique is to apply the substance by inunction to a clipped but not depilated area of the back of the guinea pig using 0 1 ml of a solution of the constituent in arachis oil. This dose is repeated daily for twenty-eight days. The guineapigs are then left for a further fourteen days at the end of which *pontamine sky blue dissolved in physiological* saline solution, is injected intravenously and two minutes later a further dose of the constituent is applied to the skin After an hour the guineapigs are killed and the skin at the site of application is reflected from the back A definite blue patch is considered as a positive reaction but a very slight blue coloration is neglected because it can be caused by excessive handling of the skin This technique was adapted from the work of Miles and Miles (1952) and Halpern (1953)
>
> In control experiments with foreign serum or chemical substances—e.g nitrosodimethylanilin and dinitrochloro benzene—which are known to produce sensitisation we obtained strong reactions by this technique The

of our work with adhesive plaster constituents are given in the following table

| *Constituent* | *Positive reactions* |
|---|---|
| Colophony | 2/10 guineapigs |
| Flectol H | 0/5 ,, |
| Chloroxylenol | 4/10 |
| Pale crêpe rubber | 1/10 |
| *Arachis-oil solvent* | 0/10 ,, |

From these results it will be seen that chloroxylenol is the most active sensitising agent, and that colophony resin and pale crêpe rubber produced a low degree of sensitisation "

In modern dermatological practice in Great Britain chloroxylenol, in the form of roxenol, is one of the commonest causes of contact eczematous dermatitis In some of the patients sensitised to chloroxylenol a history was obtained of a reaction to adhesive plaster followed by a reaction to roxenol used as an antiseptic, or vice versa, and patch-testing confirmed that it was the chloroxylenol fraction of the adhesive mass that caused the reaction We have even used plasters known to contain chloroxylenol as readily available patches for confirming sensitisation to roxenol

A patient presented with a history of a cut palm which had been treated with a well known proprietary brand of roxenol, after which a rash developed around the wound This had been treated with a roxenol ointment, and the dermatitis spread locally The patient wore cotton gloves as dressings which were immersed in roxenol by his wife before he used them Subsequently the rash developed all over both hands which became reddened, swollen, and desquamating in glove distribution with a sharply demarcated upper limit This patient also used roxenol as a shaving lotion in spite of the fact that it stung him when applied Patch tests with adhesive plaster containing chloroxylenol and another free from this substance gave positive and negative reactions respectively Subsequent avoidance of chloroxylenol brought about a steady improvement in the dermatitis

We have not yet had the opportunity to test patients with plasters modified only by the substitution of some other resin for colophony, but we have not observed any contact eczematous reaction to a plaster said to contain neither resin nor rubber

We believe that contact eczematous reactions due to plasters could be avoided, or rendered still rarer than they are, by using deproteinised rubber, by abandoning the practice of incorporating antiseptics with sensitising properties, and by substituting for colophony either a natural or a synthetic resin of lower sensitising potential

## Comments

The following difficulties may be met when interpreting results

(1) Reactions of removal and of irritation must be differentiated by inspection of the patch immediately after its removal

(2) Negative reactions with constituents and positive ones with the plaster mass may be due to some chemical interaction between constituents in the composite plaster or to the use of an unsuitable suspending agent for the ingredients under test Peck et al (1951) do not state whether the many ingredients with which they made patch tests on patients known to be sensitive to plasters were applied alone or in suspension, possibly the use of an unsuitable suspending agent may have led to their completely negative results

(3) In applying the constituents it is necessary to use an adhesive with a small sensitising potential For this purpose we have used the above mentioned plaster containing neither rubber nor resin but of relatively poor adhesive quality, on one occasion it was not even sufficiently adhesive to retain the patches in position for forty eight hours Negative patch tests have been obtained with this plaster in all cases of sensitivity to other plasters

(4) When multiple patch tests are made with plasters, if the cause is not soon determined there comes a time when the patient may begin to react in a non specific fashion to most or all of the patch test substances In these circumstances testing should be suspended for several weeks or even

## Summary

There are at least five types of reaction to adh plasters

Papulopustular reactions of irritation are more erous as the adhesiveness of the plaster is incre Other physicochemical properties of the plaster are also probably important

Reactions of eczematous sensitisation are most monly due to colophony, rubber proteins, antisepti complexes in the plaster mass Reactions to the plas or to the antioxidant have not so far been obs We have not tested our patients for sensitivity to

These reactions are rendered rarer by using d teinised rubber, abandoning the use of chlorox and substituting for colophony some other resin of sensitising potential

It is a pleasure to acknowledge the help afforded by Sm Nephew Research Ltd, who supplied much of our about substances commonly used in the manufactu adhesive plaster and provided some of the materials this investigation We also wish to thank Mr E C F for his statistical advice The photograph was take Mr P Broadbery at The London Hospital We also the many anonymous students who volunteered for p testing

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# MASKED EPILEPSY

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IN 1950 the Bristol Medico Chirurgical Society sidered at a clinical meeting a boy, aged 8½ years had recurrent attacks of pain in a leg Epilep diagnosed and confirmed by electro encephalog Later the boy began to have overt major ep attacks Treatment with phenobarbitone stopp fits and the attacks of pain

On seeing this case I first became aware that e may consist of sensory manifestations only Dur past three years, while engaged in consulting pæ practice, I have seen several cases in which assumed unusual forms, and I suspect that probably more common than is generally realised

The term " masked epilepsy " is now used to psychic seizures, psychomotor disorders, or temporary changes in personality causing aggressiveness In the past it was used in a sense, as by Sir Frederic Still (see below) Such seem to be common enough to justify resurrec the term to denote cases in which symptoms pains in the body or head, vomiting, or even are the only manifestations of epilepsy

It has long been recognised that epilepsy ma itself in various ways without convulsions or uncon ness Trousseau (1868) reported the case of a bo 10 years, who had attacks several times a day he complained of pressure in the pit of the s vomiting, giddiness, and pallor Trousseau d epilepsy but could convince no one of this until ıter when the boy had several attacks of undoubted rand mal

Sir Frederic Still (1912) wrote:

> In addition to these categories of major and minor pilepsy there is another which often passes unrecognised or a time the so called épilepsie larvée or masked pilepsy I have seen several cases in which the chief ymptom was a sudden pain in the navel or epigastrium g :—William B aged 10½, since the age of 9 months has ıad sudden attacks of pain in the epigastrium this lasts few seconds, during which there is sudden pallor succeeded y flushing after which the boy becomes pale and asks to ie down and goes to sleep for a long time This occurs everal *times a day With large doses of bromide these attacks* vere greatly reduced in number and sometimes checked ltogether for several weeks.

Kinnier *Wilson (1940) was aware of the occurrence of* uch attacks but gave his opinion somewhat cautiously

> Some of these alleged visceral equivalents might be pileptic *and not migrainous, others comparable to a tabetic* rises, still others based on unrecognised lesions.

Moore (1944 1945 1950) in America has reported everal cases which presented with abdominal pain He says:

> Most of the patients suffering from this disorder have in he past been hospitalised numerous times, subjected to scores of examinations and varied forms of therapy without relief and have had needless laparotomies done Only too frequently they have been considered as psychoneurotics or *nalingerers*

Livingston (1951) claims that Moore first described the syndrome of abdominal epilepsy This is not so *Trousseau did that seventy five years earlier*

Davidson and Lombroso (1952) described cases of epilepsy in children characterised by paroxysmal disturbances of temperature regulation producing both yperthermia and hypothermia

Mulder et al (1954) reported 100 patients who had aroxysmal visceral symptoms either as the aura of an pileptic attack or taking the place of an attack They tate

> The bizarre nature of the complaints frequently led to diagnosis of localised visceral disease Correct diagnosis lepends on the recognition of the paroxysmal occurrence of he symptoms and their inappropriateness to the total ituation together with the association of other symptoms nd findings of cerebral involvement

hey also quote Hughlings Jackson (1888) who wrote:

> The great thing as to the diagnosis of epilepsy is not the uantity of the symptoms, nor the severity of the fits, but the aroxysmalness.

In this country if the diagnosis is ever considered t all masked epilepsy is classed as extremely rare onway (1951) could find only 1 case among 250 children ged more than 2 years who attended as outpatients t The Hospital for Sick Children Great Ormond Street ondon with abdominal pain as the main complaint he six most common diagnoses were as follows

| *Diagnosis* | No *of cases* |
|---|---|
| Colic of unknown cause | 73 |
| Mesenteric adenitis | 54 |
| Constipation | 48 |
| Periodic syndrome | 21 |
| Psychogenic | 23 |
| Enteritis | 13 |

Perhaps the colics of unknown causation periodic ndromes and psychogenic cases *concealed a few* fferers from masked epilepsy

## Case reports

### SO-CALLED CYCLICAL VOMITING

**Case 1**—A boy aged 8 years came to my notice when his ster was brought into hospital with status epilepticus rom the age of 2½ years he had had recurrent attacks of vere vomiting Sometimes during these he became unaware his surroundings for as long as thirty minutes and occasionally the right side of his face twitched His mother was alive and well His father had occasional bilious attacks His sister was aged 6 years and had had two attacks of *vomiting and unconsciousness on previous occasions* The boy had been seen once by a consultant who wrote From the family and personal history I guess this is a form of cyclical vomiting which may well lead on to migraine later in life When his sister came into hospital it was found that she had epilepsy and it was decided to investigate the boy also

*On examination* he showed no abnormal signs in the central nervous system. His blood pressure and urine were normal The Wassermann reaction was negative and radiography of the skull showed no abnormality An electro-encephalogram showed a highly abnormal record indicative of epilepsy; there were no focal or localised abnormalities.

*Treatment* with phenobarbitone has controlled the attacks and when he is given gr 1½ daily he has no trouble

*Comment*—*The history of unconsciousness and twitch*ing of the face should have stimulated further investigation which would have led to the correct diagnosis earlier The epilepsy can scarcely be called masked but merely unrecognised

**Case 2**—A girl suffered from frequent bilious attacks from *the age of 8 years. Her father had had similar attacks in* childhood She had several attacks of acute tonsillitis and in January 1949 her tonsils were removed In March 1949 she developed acute nephritis and was admitted to hospital The disease ran a mild course and she was discharged after seven weeks, apparently cured The registrar's summary of her stay stated She has been inclined to get attacks of vomiting associated with pyrexia up to 102 F for which we have been unable to find any very satisfactory cause At home she continued to have bouts of pyrexia and vomiting Sometimes these were accompanied by right-*sided headache and twice she had what were termed black* outs Her family doctor sent her to a consultant as a case of cyclical vomiting No abnormal physical signs were found apart from carious teeth and no firm diagnosis was made Later the attacks were accompanied by severe lower abdominal pain and diarrhœa The family doctor then referred her at the age of 12 years, for a further opinion He thought that the attacks did not fit in with cyclical vomiting but were psychological in origin though he admitted that he could detect no cause of mental conflict Further questioning of her mother revealed that during the attacks *she usually became unresponsive sometimes unconscious* and occasionally incontinent of urine The family doctor had given her phenobarbitone gr ¼ daily for six months and during that time she was free from attacks For some reason he stopped it and the attacks returned

*Investigation* showed no abnormality in the central nervous system, blood pressure urine radiograph of skull or Wassermann reaction An electro encephalogram showed an abnormal record indicative of epilepsy there were no focal abnormalities, nor was there any lateralisation

*Treatment*—She was treated with phenobarbitone and had *one attack of vomiting in two years* A second electro encephalogram taken eighteen months after the first showed some epileptiform features but there is considerable improvement since the previous record the patient would appear to be well controlled by anticonvulsant drugs

*Comment*—The epilepsy was masked at first and caused attacks of pyrexia and vomiting Later the clues of unconsciousness incontinence and improvement under treatment with phenobarbitone led to a diagnosis of epilepsy even before the electro-encephalogram was taken It seems that pyrexia may be one of the manifestations of epilepsy It might be argued that the pyrexia caused the epilepsy; but no explanation was found for the pyrexia though by chance it was observed in hospital while she was suffering from another disease In fact the pyrexia took the place of convulsions

### HEADACHES

**Case 3**—A boy aged 4 years with no relevant family history was sent into hospital because of attacks of headache sleepiness and vomiting which had begun at the age of 1 year and had recently become more frequent At first there were intervals of 4 6 months between the attacks but just before his admission he had three attacks in fourteen days The onset was with headache after about thirty minutes he went to sleep at intervals he woke up and vomited, then went back to sleep He became pale, yet his skin was hot and perspiring There was no correlation with the time of day, meals or exercise

*Examination and investigation* revealed no abnormality His blood sugar level three hours after a meal was 108 mg per 100 ml An electro encephalogram showed a record just outside normal limits with mild epileptiform features, but it is not indicative of this condition , there were no focal abnormalities "

*Treatment* —Since it was felt that the attacks were probably epileptic, he was treated with phenobarbitone, and after three months he was much improved His mother stated that he had had no attacks at all and that he was " a different child " She also said that he used to grunt and nod his head when asleep but did so no longer

*Follow up* —Another electro encephalogram, taken three months after the first, showed ' a record which remains outside normal limits and is now definitely suggestive of epilepsy '

**Case 4** —A girl had, at the age of 5 years, a febrile illness which was not diagnosed For three months after this she complained of headaches at intervals of about a week During the attacks she lost her appetite, became pale, and felt sick, but did not vomit She had had two convulsions in infancy which were ascribed to teething and were ignored Her brother, aged 17 months, had already had one convulsion Her mother had had shock therapy for schizophrenia, and a first cousin on her mother s side had epilepsy

*Examination and investigation* revealed no abnormality except possibly that some increase in intracranial tension was visible in the radiograph of the skull There was no papillœdema An electro-encephalogram showed " an abnormal record indicative of epilepsy , there were no focal or localised abnormalities "

*Treatment* —The girl was treated with phenobarbitone After three months her mother reported that the headaches were less frequent, and after another three months they had disappeared The mother then volunteered the statement ' She is not the same child She is not noisy and mischievous any more She used to get panic stricken but doesn't now "

*Comment on cases 3 and 4* —Note the alteration in behaviour observed by the parents when these two children were treated adequately The idea of an epileptic personality as a precursor to epilepsy has been discarded, but these two cases suggest that there may be such an entity It is possible that personality changes may be the only manifestation of epilepsy

**Case 5** —A boy, aged 9 years, had three years' history of headaches They occurred every day and lasted from one to twelve hours He went pale but had no nausea or vomiting Neither aspirin nor codeine tablets relieved him At the age of 2 years he weighed only 21 lb and was referred to a consultant, who found no abnormal physical signs and made no investigations or diagnosis His mother had had fits up to the age of 7 years

*Examination* revealed a small boy weighing 44 lb , but no other abnormalities except a positive tuberculin test and a doubtfully opaque left antrum on radiography An ear, nose, and throat surgeon considered this last finding of no importance The Kahn test was negative The boy was sent home from hospital with no definite diagnosis

*Later history* —He continued to have headaches, though not so often as before A year later he began to vomit, and epilepsy was considered Electro encephalography showed an abnormal record definitely suggestive of epilepsy , although there was some localisation to the parieto temporal lobes with a left sided preponderance, the degree of asymmetry was not great '

*Treatment* —He was treated with phenobarbitone His headaches became fewer but, when they did occur, more severe An attempt was made to use primidone, but this was abandoned because of the side effects The use of sodium phenytoin in addition to phenobarbitone has proved successful

ABDOMINAL PAIN

**Case 6** —A boy aged 8 years whose mother suffered from migraine had sick headaches for two years and then had one which was accompanied by abdominal pain He was surgeon who stated that there was no appendicitis

Later on he was investigated in the pædiatric outpatient department, and no abnormality was found in any system Migraine was tentatively diagnosed It was suggested that either codeine or ergotamine might be tried During the next eighteen months he had repeated attacks of vomiting and abdominal pain There was no relief from codeine Ergotamine was not tried He was an only child, and his family doctor felt that his troubles might be magnified by his mother He sent him to another surgeon for advice about the appendix This surgeon too refused to operate, and the boy was refer to the medical side again

*Investigation* revealed no abnormality, but it was consider that the abdominal pain might be an epileptic equivale An electro encephalogram showed " a definitely abnor record indicative of epilepsy , there were no foc abnormalities "

*Treatment* —The boy was treated with phenobarbitone and during six months has had no attacks

*Comment* —But for the vigilance of two surgeons the boy would probably have had a normal appendix removed This case shows the importance of full investigation even in cases where there is every reason to suspect that psychological difficulties are concerned

**Case 7** —A girl, aged 5 years, was referred by the school doctor for attacks of abdominal pain which was severe enough at times for her to be sent home from school She had had them since the age of $2^{1}/_{2}$ years They came on about th or four times a week, making her scream She felt sick bu never vomited One of her mother's brothers had had simil symptoms in childhood, and at the age of 20 began to hav epileptic fits, which continued at intervals for thirty years

*Investigation* revealed no abnormality apart from larg tonsils The report on the electro encephalogram was " This is an abnormal record definitely suggestive of epi There were no focal abnormalities "

*Treatment* —The girl was treated with phenobarbitone has remained remarkably free from pain After a month treatment her mother said " She has not complained anything for four weeks, which is quite unusual for her '

## Discussion

### *Diagnosis*

It seems fair to say that the main symptoms in idiopathic epilepsy may be headaches, or vomiting, pains, or pyrexia, or a combination of any of They do not represent an aura but take the place of th convulsion and unconsciousness as epileptic manifestations If a child has any of these symptoms at intervals or for a long period and they cannot be explain an electro encephalogram should be taken Points the history which suggest epilepsy are a family tend to convulsions, pallor during the attacks, drowsine after them, and improvement when treated with anticonvulsants , but it is not necessary for these to present before pressing on with the investigation Th is, of course, no excuse for neglecting to make a th investigation to exclude other causes of the sympto In some cases pyrexia acts as a trigger for an attack epilepsy, and the cause of the pyrexia must be sou In all cases the possibility that a cerebral tumour m cause the symptoms must be borne in mind and exclud before idiopathic epilepsy is diagnosed

Patients are sometimes seen in whom a firm diagno of grand mal or petit mal is made but no abnorma is ever recorded in their electro encephalographic tracin Presumably the same may happen in masked epilep The diagnosis is then very difficult , but it may be m if there is a strong family history and the response treatment is satisfactory

### *Family History*

Of the 7 children reported here 4 had a history convulsions in near relations In addition a parent 1 of them had had recurrent vomiting in childho and a parent of another child had migraine In 1 case could no relevant family history be obtai In cases 1, 2, 6, and 7 there was a story of similar att which might have been masked epilepsy, in relations

*Age of Onset*

The age of onset varied from 1 to 8 years which is consistent with the usual onset of idiopathic epilepsy 'Three months' colic' investigated by Illingworth 1954) seems to be a baffling disease and it might be worth considering whether it is sometimes due to epilepsy Illingworth cites Still and Sheldon as stating that it sometimes leads to convulsions No cases of three months' colic have been met with in this nvestigation

*Treatment*

In this series phenobarbitone has generally proved successful in relieving symptoms In America either diphenyl hydantoin sodium or a combination of drugs is usually recommended. Blumberg (1954) describes a case where troxidone proved necessary This patient who had become a problem child was, when his abdominal epilepsy was controlled converted into a joy and a model child.'

It seems best to try first the least toxic drug available —i e phenobarbitone—and to give it in adequate doses Epileptic children seem able to tolerate large amounts of phenobarbitone without becoming sleepy whereas normal children cannot

*Incidence*

These 7 cases were met with in three years' consultant pædiatric practice, during which about 1400 new patients were seen either as outpatients or on admission to hospital The figures are of little value, however because in the early months cases must have been missed and classed as psychogenic or inexplicable, whereas later when general practitioners had realised my interest in such cases they might refer more than would normally come into the net A few more cases have been seen recently but have not been followed up long enough to merit nclusion here

*Cyclical Vomiting*

It is doubtful if this disease exists No genuine cases have been seen in this area in the past three years Investigation may reveal one of the following causes Abortus fever cerebral tumour islet-cell tumour of the pancreas recurrent neutropenia recurrent pyelitis, sinusitis or tuberculous mesenteric adenitis

In the first description of cyclical vomiting (Gee 1882) cases were reported of fitful or recurrent vomiting The notes nowadays would be judged inadequate but some of the patients may well have been epileptic Of the 5 for whom a family history was given 4 had near relations who had paroxysmal headaches or megrim

Hamilton (1951) has pointed out that one or other of the parents is not infrequently a victim of migraine Smith (1951) gave his experiences with 700 public school boys 108 of them had had attacks of vomiting before entry at the age of 13 and 13 of these developed migraine Smith stated

> The most dramatic migrainous sequel is epilepsy One boy who had habitual and often violent sick headaches suddenly had a severe epileptic fit in the school library He was treated with sedatives and had no further attacks

The only other boy who crossed the frontier from migraine to epilepsy continued to have attacks, because his father a well known surgeon (who had had similar attacks until the age of 17) was against phenobarbitone

These two (or three if we include the father) might well be called cases of masked epilepsy

*Migraine*

The relation between migraine and epilepsy has been described often enough and the electro encephalogram in migraine has been studied It is usually stated that the tracing is abnormal but not typical of epilepsy The main difficulty has been in diagnosing migraine accurately The cases and families described above seem indicate that two conditions cause paroxysmal headaches true migraine and masked epilepsy To the unsuspecting observer masked epilepsy will often seem to be migraine and no doubt in the past many cases have been so labelled

This surmise is supported by the following statement made by Critchley (1950)

> Prevention of attacks of migraine by medicinal means is often most disappointing Perhaps phenobarbitone is the safest bet Little if any benefit results from the administration of this drug at the time of an attack. The patient should persevere for two or three months before concluding that the drug is without avail

*Night Terrors*

It is well recognised that these are sometimes epileptic manifestations (Paterson 1944) In giving the history of patients with epilepsy parents often make some such statement as He sleeps badly, He is on the go all the time in his sleep ' and He jerks and twists about in bed " In some cases there is a history of this unrest at night in brothers or sisters who show no other indication of epilepsy Treatment with phenobarbitone usually controls it

*Electro-encephalography*

It is usually conceded that a normal tracing can be obtained from an undoubted epileptic and that a normal person may at times show an abnormal tracing, though with modern techniques this is becoming rarer Critics may complain that this makes it easy to invent a syndrome and to call it masked epilepsy The proof of the pudding is in the eating The considerable improvement which took place in these patients when they were treated with phenobarbitone confirms the epileptic nature of their illness Moreover none of them fitted any other diagnosis

Of the 7 cases 6 had no localising features but in case 5 the parietotemporal lobes seemed to be involved It is doubtful if localisation is of any value in this condition, though Mulder et al (1954) suggest that it may be

*Nocturnal Enuresis*

It has been suggested that nocturnal enuresis may in some patients be the only symptom of epilepsy Turton and Spear (1953) found an abnormally high percentage of epileptic tracings in a survey of 100 children who had severe enuresis Treatment with phenobarbitone rarely benefits such patients and the question may be considered to be still unsettled

*Psychological Causes*

Fielding (1749) wrote

> Every physician almost hath his favourite disease to which he ascribes all the victories obtained over human nature The gout the rheumatism the stone the gravel, and the consumption have all their several patrons in the faculty : and none more than the nervous fever or the fever on the spirits

The fashion has not altered, and nowadays abdominal pain is often put down to psychological causes Certainly pain in children sometimes has a psychological cause or reason for continuing but this is not common. It is very easy to call pain psychological whenever we do not understand its nature (cf Moore 1944 1945 1950) The state of a child who has a genuine pain which his parents and doctor cannot explain is sad indeed and after the passage of time he may well become neurotic Let us therefore seek ever more earnestly for causes and see if we cannot whittle down the core of abdominal pain of unknown origin.

*Telling the Parents*

People still have fear and horror of the word epilepsy Fits convulsions and seizures may be allowed but epilepsy not It is difficult to explain masked epilepsy to some parents and occasionally they will aggressively resist it Either we can attempt to educate parents into a realisation that epilepsy is not a slur nor inevitably associated with mental deficiency or we can glide over the problem by using such terms as "abdominal migraine"

### Summary

Cases are described in which epilepsy manifested itself as pain in the leg, so called cyclical vomiting headaches, pyrexia, and abdominal pain

This type of epilepsy is fairly common though often unrecognised, and many cases of cyclical vomiting and migraine may prove to be epileptic

The term "masked epilepsy" should be extended to include these phenomena

Treatment with phenobarbitone is usually successful

I wish to thank Dr H Lovell Hoffman for advice, and Dr E C Turton for his reports on the electro encephalograms

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# SUBACUTE COMBINED DEGENERATION OF THE SPINAL CORD

## WITH MEGALOBLASTIC ANÆMIA DUE TO SPONTANEOUS ILEOCOLIC FISTULA

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This is the first recorded example of subacute combined degeneration of the spinal cord with macrocytic anæmia and spontaneous ileocolic fistula Initially liver therapy cured the anæmia and arrested the neurological degeneration, and this position has been maintained without further liver injections after successful resection of the fistula The 3 published cases of anæmia and subacute combined degeneration of the spinal cord due to intestinal fistula all followed gangrenous appendicitis and all were fatal In the present case the discovery of the fistula after a barium meal rather than an opaque enema is unusual Free hydrochloric acid was present in the gastric juice, and there was an increased amount of fat in the stools Diarrhœa was not a prominent symptom The clinical picture was complicated by a duodenal ulcer

### Case-report

A woman aged 25 whose mother had died of pernicious anæmia, was first seen in 1941 complaining of nausea and vomiting shortly after meals During the next two years she lost 2 st in weight, and in 1943 an active duodenal ulcer was found radiographically, associated with normal acid secretion In April 1945, the patient complained of breathlessness difficulty in walking and a feeling of uselessness in the legs, hands and arms Her diet since 1943 had consisted mainly of eggs and milk

*On examination* she was pale and thin with bruising over the lower back and knee joints There was moderate pitting œdema of the ankles The liver was palpable one fingerbreadth below the costal margin The knee jerks and ankle jerks were absent, and the plantar responses were extensor [illegible] considerable disturbance of joint and position [illegible] lower and upper limbs and vibration sense was absent in the legs up to the level of the iliac crests Romberg's sign was positive No other abnormality was found

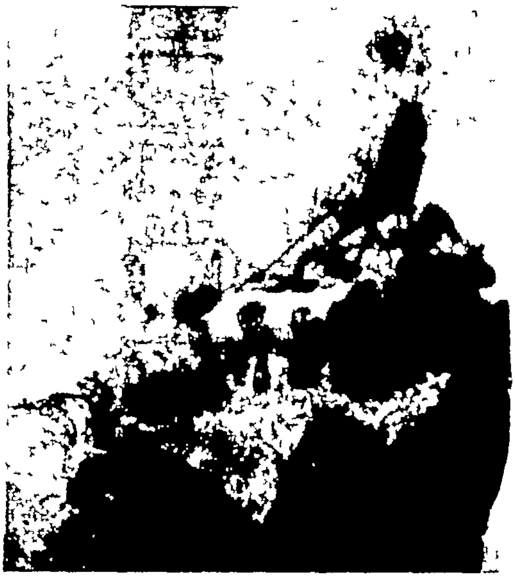

Fig 1—Film three-quarters of an hour after barium meal, showing communication between small bowel and middle of transverse colon and diverticula in small bowel

*Investigations*—Examination of the blood showed red cells 1,150,000 per c mm, with anisocytosis megalocytosis, and polychromasia, Hb 32% (4 9 g per 100 ml), white cells 2000 per c mm, Arneth shift to the right A van den Berg test gave a positive direct response Sternal puncture showed megaloblastic hyperplasia Fæcal fat on a normal diet was 76% and 28% of the dry weight of two random specimens Blood ascorbic acid 0 14 mg (normal 0 75 mg) per 100 ml Serum iron 26 8 µg (normal 98–112 µg) per 100 ml Plasma proteins 5 3 g per 100 ml albumin/globulin ratio 1 1/1 A test-meal showed that free hydrochloric acid was present.

*Treatment and Progress*—The patient was treated with crude liver extract parenterally and had a reticulocyte response of 34% the Hb increasing to 60% in a month by November, 1945, the blood picture was normal. At that time a further barium meal and follow through radiological examination was made which showed, in addition to the chronic duodenal ulcer, an ileocolic fistula and several diverticula scattered through the small intestine (fig 1) A contrast enema showed a doubtful irregularity in the middle of the transverse colon Treated with liver the patient remained well except for occasional attacks of mild diarrhœa lasting two or three weeks every two or three months. Medical treatment improved the abnormal neurological signs but did not entirely abolish them, with the result that by August 1948, the plantar responses were less briskly extensor, and sensory disturbance was limited to loss of vibration sense below the knees Repeat barium studies in November, 19 confirmed the presence of the fistula At that time the patient weighed 114 lb, her Hb was 94% (14 g per 100 ml) with normal red cell morphology, and the plasma protein was 6 5 g per 100 ml, with albumin/globulin ratio 1 The colloidal gold reaction of the serum was negative The total fæcal fat in a twenty four hour specimen was 46 0% of the dried fæces (on a normal diet)

*Operation*—The fistula was excised by Mr J C An F.R C S on Jan 22, 1951, and the peritoneal cavity was found to be obliterated by fine avascular adhesions Directly below the incision a fistula was found from the middle of the transverse colon to a loop of small bowel which could not be identified The fistula was excised and the normal continuity of the bowel restored

*Postoperative recovery* was uneventful and the patient was discharged ten days after the operation, liver treatment being discontinued

*Follow up*—The patient was seen again on March 12 1954 when she reported that she was very well and had gained a little weight Her red cells were 5,600,000 per c mm, with normal morphology, Hb was 94% (14 g per 100 ml), eucocytes were 5600 per c.mm. The neurological signs were unchanged. On March 15, 1954, her weight had increased to 140 lb. and she was in full-time employment. She had no nausea or vomiting and her bowels were regular with no diarrhœa. Her plantar responses were equivocal and her only sensory abnormality was some diminution in vibration sense over the lower legs. Her Hb was 84% (12·4 g. per 100 ml.) and the red-cell morphology was normal.

## Discussion

The presence of free acid in the gastric juice excludes the diagnosis of pernicious anæmia. Askey (1944) carefully reviewed 47 reported cases of pernicious anæmia with free acid and found none proved. The association of macrocytic anæmia with lesions of the bowel has been recognised for more than fifty years, cases being reported by White (1890), Wallis and Warfinge (1893), and Meulengracht (1929); but Faber (1895) seems to have been the first to suggest a causal relationship (Plum and Warburg 1939). The first recorded instance of macrocytic anæmia following intestinal anastomosis appears to be that of Little et al. (1929). The subject of macrocytic anæmia with intestinal stricture and anastomosis is well reviewed by Barker and Hummel (1939), who add 2 new cases and give details of 40 previously reported examples. Cameron et al. (1949) found 9 more patients in the published reports of the next decade and added 1 of their own. Wilkinson (1949) states that all cases of intestinal macrocytic anæmia would respond to liver if the marrow were megaloblastic, and this was the experience in the present case.

The combination of bowel lesion, macrocytic anæmia, and involvement of the spinal cord is much less common. Davis and Brown (1952) say of megaloblastic anæmias resulting from structural abnormalities affecting the small intestine: "Neurological complications are extremely rare, but a few cases have been recorded." Watson and Witts (1952) state that subacute combined degeneration of the cord occurs "in a fairly large proportion of patients," but give no details. However, in an earlier analysis of published cases Cameron et al. (1949) found "neurological signs" in 12 of 61 cases. This total includes 2 patients with subacute combined degeneration.

The first of these (Little et al. 1929) was in a man aged 20 who had two entero-anastomoses for intestinal obstruction following gangrenous appendicitis and who also had fæcal fistulæ. A macrocytic anæmia with normal gastric analysis developed. The anastomoses were undone and the diarrhœa ceased, but further treatment of the macrocytic anæmia with liver was necessary. On two occasions withdrawal of treatment was followed by relapse, and on the second of these the patient developed "combined system disease" and died; necropsy showed obstruction from adhesions.

The second, a patient of Hurst (1933), was a woman aged 30 with symptoms of intestinal obstruction following appendicectomy. She was treated by ileocolic anastomosis, and five years later she developed severe macrocytic anæmia with free acid in the gastric juice and signs of further obstruction. She had bilateral extensor plantar responses and diminished knee-jerks and ankle-jerks, with pins and needles in feet and hands. She died three weeks after operation for relief of the obstruction. There is no mention of a necropsy.

Woltman and Heck (1937), reviewing degeneration of the spinal cord in conditions other than pernicious anæmia, gave details of a woman aged 60 who developed multiple intestinal fistulæ and a fæcal fistula after appendicectomy. Later the hæmatological and neurological picture of pernicious anæmia developed, and typical subacute combined degeneration of the cord was verified at necropsy. There is no mention of any gastric analysis; therefore the concurrent development of true Addisonian anæmia cannot be entirely excluded.

Of 8 patients with short-circuits and intestinal loops were deficient in vitamin $B_{12}$ and hence potential candidates for degeneration of the spinal cord (D. L. Mollin, personal communication). Thomson (1953) describes a man aged 20 with ileocolic anastomosis following appendicitis and macrocytic anæmia but no neurological involvement. The anæmia was cured with vitamin $B_{12}$, and, later, operation to restore normal bowel continuity made further treatment with vitamin $B_{12}$ unnecessary. In an analysis of the "intestinal loop syndrome" Jackson and Linder (1951) conclude that involvement of the upper end of the small gut tends to produce predominantly steatorrhœa, and of the lower end predominantly anæmia. From the present review it seems that neurological complications, when they occur, are also commonest with lesions of the lower part of the small intestine.

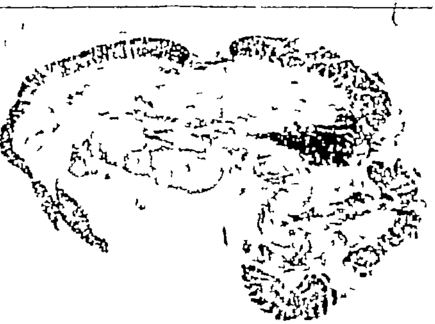

Fig. 2—Section through fistula, showing absence of Crohn's disease and of tuberculosis. (× 8.)

The ætiology of the fistula in the present case remains obscure. Taylor (1930) found at necropsy of a woman aged 54 with macrocytic anæmia and multiple intestinal diverticula the peritoneal cavity almost obliterated by adhesions, as in the present case, presumably due to past inflammation. Perforation of one of the small-bowel diverticula into the colon seems the most likely cause of the fistula in the present case. There was no histological evidence of Crohn's disease or of tuberculosis (fig. 2).

## Summary

A case of subacute combined degeneration of the spinal cord with macrocytic anæmia following the development of an ileocolic fistula of unknown cause is reported.

The fistula was demonstrated by a barium meal but not by an opaque enema.

The anæmia and the spinal-cord disease were arrested by treatment with liver extract. Resection of the fistula completed the cure, doing away with the need for further liver injections.

Three years after operation the patient is well and has a normal blood count.

I wish to thank Dr. H. S. Kellett for the hæmatological findings, Dr. R. J. C. Campbell for the radiograph, and Dr. R. E. Steiner for advice and encouragement.

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# PAPAIN-TREATED RED CELLS IN THE DETECTION OF INCOMPLETE ANTIBODIES

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PROTEOLYTIC enzymes modify red cells so that they can be agglutinated in saline suspension by incomplete rhesus antibodies Following work with cholera filtrate by Pickles (1946) Morton and Pickles (1947) described the use of trypsin for the purpose and later (Morton and Pickles 1951) described the use of a filtrate of *Streptomyces albus* extract and briefly mentioned tests using papain Kuhns and Bailey (1950) reported on papain more fully The technique described below, modified from that of Kuhns and Bailey, has proved both reliable and delicate Stratton (1953) introduced a slide technique using papain treated red cells The method he recommended was used in parallel with the tube technique in the examination of 110 sera

The use of papain treated cells obviates certain objections to other methods of detecting antibody prozone effects, the formation of rouleaux in protein and other colloidal media, the expense of commercial bovine albumin, and the time and skill needed to produce the anti-human globulin serum of Coombs et al (1945)

## Reagents

*Stock Papain*—1 g of papain is suspended in 100 ml of 0 85% sodium chloride It may be stored for several months at +4°C Eleven brands of papain were tested All appeared reliable, but those of Biddle, Sawyer * and of Mawson † appeared the most active for the purpose

*Preparation of Papain Solution*—As an alternative to the papain suspension described above a more elegant preparation in the form of a solution may be obtained as follows Stock papain suspension is stored at +4°C for twenty four hours care being taken to agitate it at intervals It is then centrifuged, and the supernatant fluid is retained for use in exactly the same way as the suspension The solution is slightly less active than the suspension but has proved wholly reliable

*Storage of Stock Papain for Long Periods*—Whereas stock papain in current use keeps best at +4°C, thus eliminating the need for constant freezing and thawing, the stock reagent will keep for long periods at −20°C It has been found useful to store at −20°C the bulk stock papain, be it suspension or solution A small quantity at a time is thawed out and kept at +4°C for routine use

*Stock Buffered Saline Solution*—1 volume of 1/15 molar Sorenson phosphate buffer, pH 7 3, prepared by adding 3 parts $M/15$ $Na_2HPO_4$ to 1 part $M/15$ $KH_2PO_4$, is added to 9 volumes of 0 85% sodium chloride solution

*Red Cells for Treatment*—Red cells, both group O rhesus positive (CDe/cDE, $R_1R_2$) and group O rhesus negative (cde/cde,rr) are washed three times in 0 85% sodium chloride solution After the last washing they are packed

## Method

Nine volumes of stock buffered saline solution are added to one volume of stock papain To one volume of the thrice-washed packed rhesus-positive cells and to one volume of the thrice washed packed rhesus negative cells are added in each case two volumes of the buffered saline papain mixture The cell suspensions so prepared are incubated for thirty minutes at 37°C in a water-bath The cells are next washed three times and made up to a 5% concentration in 0 85% saline solution Before use they are warmed to 37°C

0 1 ml of the serum to be tested is pipetted into each of two "precipitin" tubes (7 × 50 mm) and warmed to 37°C in the water-bath This eliminates the non specific agglutination shown by many sera of enzyme-treated red cells at +20°C or less 0 1 ml of the enzym treated rhesus positive cell suspension is added to o of the two precipitin tubes, and a similar quantity o the rhesus-negative cells to the other After an hour incubation at 37°C the two tubes are read macrosco cally and checked microscopically for the presence o agglutination, care being taken not to let the red ce cool during the process Microscope slides warmed t 37°C may be used to lessen the degree of false posi results due to cold agglutinins

## Results

61 sera containing rhesus antibody were ex On no occasion was macroscopical agglutination abse In each case a papain treated red cell titration was do and parallel titrations were done with red cells suspende in saline solution and in 20% bovine albumin, and b the anti-globulin technique of Coombs et al (1945) a the trypsin and *Strep albus* techniques of Morton an Pickles (1951)

110 maternal sera were examined by Stratton's technique in parallel with the papain method describe above and with the other methods mentioned 5 specimens gave a false positive result by Stratton's method all other methods used in parallel being negative Th technique, when antibody titrations were compared seemed to be as sensitive as the tube papain te described in this paper

The tube technique with papain-treated red ce proved as sensitive as any other method, giving ve few false positive results The table gives examples results obtained with four typical anti Rh sera

EXAMPLES OF TITRATION OF FOUR RHESUS ANTISERA

| — | Rhesus antiserum | | | |
|---|---|---|---|---|
| | 1 | 2 | 3 | 4 |
| Saline solution | 0 | 0 | 1 | 0 |
| 20 % bovine albumin | 2 | 8 | 2 | 1 |
| Anti globulin test (Coombs et al 1945) | 2 | 8 | 8 | 3 |
| Trypsin technique (Morton and Pickles 1951) | 4 | 32 | 16 | 6 |
| *Strep albus* technique (Morton and Pickles 1951) | 4 | 64 | 16 | 6 |
| Papain technique (tube method) | 8 | 512 | 16 | 1 |
| Papain technique (Stratton 1953) | 8 | 256 | 16 | 1 |

In 3370 maternal sera examined papain gave o 11 false positive results and no false negatives It believed that most false positive results develop a result of cooling of the cell serum mixture Of the fa positives only one was detected on repeating the t again with the same reagents During tests with papa treated red cells in other blood group systems enhanc ment of agglutination was noted with Anti-A, Anti Anti M, Anti N, Anti $Le^a$, and Anti $Le^b$ No agglutinati took place with Anti $Fy^a$

## Discussion

The method described has certain advantages o *other antibody techniques in routine use The format* of rouleaux, common in protein media, is obviat Papain is much more economical than the relativ expensive commercial bovine albumin Moreover t considerable time and skill required for the p of anti-human globulin used in the Coombs techni is avoided Papain appears more sensitive than eit trypsin or *Strep albus* The method described is simp than that of Kuhns and Bailey (1950), for they rec mend continual agitation of the cell suspension dur the time that it is being treated with the enzyme, a suggest centrifuging the tubes containing cell s mixture before finally reading the results Both th requirements have been eliminated

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In Stratton's method it is necessary to prepare an activator fresh on the day of use. This was also found unnecessary moreover the error due to false positives was rather higher than in the tube method.

## Summary

A method is described for the preparation and use of papain treated red cells to detect incomplete rhesus antibody.

Results of testing 3370 maternal sera are considered as well as the titration of 61 rhesus antibodies. Mention is made of reactions with papain treated red cells in other blood group systems.

The papain technique appears very reliable and more sensitive than any other for routine use in the detection of incomplete rhesus antibodies.

Thanks are due to Prof R J V Pulvertaft Dr A E Mourant and Dr J G Humble for very helpful advice and criticism and to Dr Mourant for the various antisera.

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# PRIMARY PEPTIC ULCERATION OF THE JEJUNUM

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WHEREAS *ulceration of the jejunum* as a sequel to gastro-enterostomy is so common as to bring that operation for the treatment of duodenal ulcer with hyperchlorhydria into universal disfavour primary jejunal ulceration is distinctly uncommon.

The first description of *primary jejunal ulceration* was attributed by Ebeling (1933) to Sostier (1827). Richardson (1922) reviewed 12 published cases and added 1 of his own; Ravdin (1927) brought the tally up to 23; and Ebeling (1933) reviewed 47 cases. Berry and Dailey (1940) brought to light 9 other published cases which had been missed; and these, their own case, other cases subsequently published (Robinson and Wise 1940, Dowdle 1942, Chambers 1943, Carmichael and Doggett 1946, Evert et al. 1948) and the present case bring the total number of published cases to 83.

Primary jejunal ulcers behave in every respect like peptic ulcers of the lesser curvature of the stomach or the first part of the duodenum inasmuch as they may cause symptoms of dyspepsia and may bleed, perforate, or stenose. Both the practical considerations of natural history and management and the theoretical consideration of ætiology of primary jejunal ulceration are well illustrated in the ensuing case.

## Case report

A married woman aged 23 first began to complain of ulcer pain in 1951. She had previously been healthy if rather delicate. The only relevant past history was of amenorrhœa associated with an infantile uterus and attributed to ovarian insufficiency. In January 1951 she complained of epigastric pain and heartburn coming on two or three hours after a meal and relieved by food and alkalis. In February 1951 when she presented herself as a blood-donor she was rejected on the score of anæmia.

Early in 1952 she became weak and noticeably more pale and her attention was drawn for the first time to the passage of tarry stools. Her dyspeptic symptoms had meanwhile subsided but in February 1952 she had an attack of severe upper abdominal pain lasting three days. Her hæmoglobin was only 5 g per 100 ml and she was given blood transfusions. Barium meal radiography at that time is said to have indicated a possible ulcer in the second part of the duodenum (fig 1) but a further radiograph taken two weeks later did not confirm this finding. During the ensuing three months she continued to have intermittent upper abdominal pain.

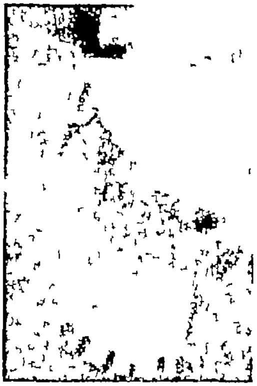


Fig. 1—Barium-meal radiograph in January 1952 showing apparent ulcer crater in second part of duodenum. This crater was not seen in barium-meal radiograph two weeks later.

*First Admission and Laparotomy.*—In May 1952 she was admitted to the Royal Perth Hospital after a very severe attack of melæna. She was a thin frail girl of considerable intelligence but displaying a child-like dependence on her dominating mother. Physical examination was unrevealing. The abdomen was lax and not tender. A fractional test meal showed an exceptionally high level of acid secretion, free HCl rising to 100 clinical units at the end of the first hour without histamine stimulation. Barium meal radiography (fig 2) showed some distension of the duodenum and jejunum, the significance of which was unapparent. The proximal jejunum did not show active peristalsis.

Laparotomy confirmed the duodenal dilatation but no bowel lesion was detected and no active surgical measures were undertaken.

*Second Admission.*—In September 1952 further upper abdominal pain was followed by a severe hæmatemesis. No abnormality of the stomach was disclosed at gastroscopy.

*Third Admission.*—Early in 1953 the patient complained again of epigastric pain occurring two hours after meals and radiating into the back. The pain was not now relieved by food or by alkalis. After another attack of melæna she was readmitted and given blood transfusions. Barium meal radiography and gastroscopy were unrevealing and a cholecystogram was normal. Overnight gastric secretion, followed by a histamine test meal in the morning, was studied. The results are shown in figs. 3 and 4. Total nocturnal secretion of gastric juice and HCl production exceeded even the mean values obtained by Levin et al (1952) in male patients with duodenal ulcers. Before this admission the patient had also complained of loose motions passing two or three bulky pale offensive stools daily. The suspicion of steatorrhœa was not confirmed for on a daily intake of 160 g of fat 90% was absorbed.

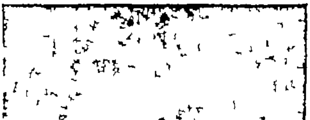


Fig 2—Barium-meal radiograph in May 1952, showing considerable dilatation of second and third part of duodenum

*Fourth Admission and Second Laparotomy.*—Further pain

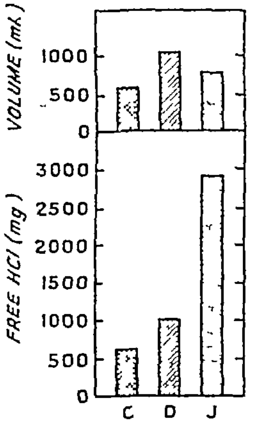


Fig 3—Volume of and amount of free HCl in gastric juice secreted from 9 p m to 9 a.m by controls (C), male patients with duodenal ulcer (D) (Levin et al 1952), and patient with primary jejunal ulcer (J)

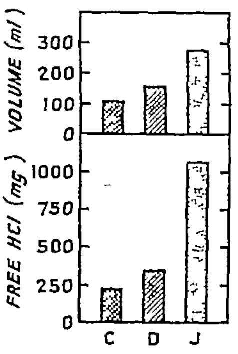


Fig 4—Volume of and amount of free HCl in gastric juice secreted in 1 hr after histamine stimulation in controls (C), male patients with duodenal ulcer (D) (Levin et al 1952), and patient with primary jejunal ulcer (J)

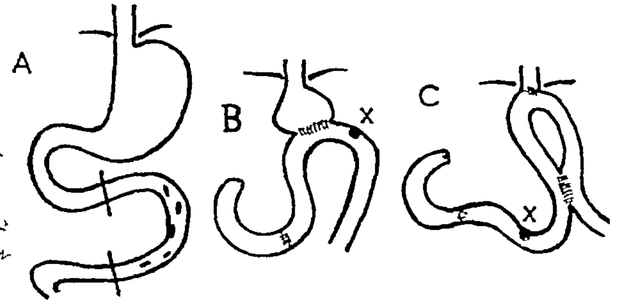
and hæmatemesis occurred in October 1953 Gastroscopic appearances of the stomach were again normal Several hours after gastroscopy the patient complained of acute generalised abdominal pain Examination showed distension and abdominal rigidity The radiological demonstration of gas under the diaphragm confirmed the diagnosis of perforation of the bowel

At laparotomy (Mr Hector Stewart) a perforation of the jejunum on its antimesenteric border about 10 cm distal to the duodenojejunal flexure was found The edges felt indurated, suggesting perforation at the site of the ulcer What was thought to be another ulcer was palpated about 6 cm proximal to the site of perforation The stomach was normal The duodenum was greatly dilated The ulcer was oversewn, and the abdomen was closed without drainage

*Fifth Admission and Third Laparotomy*—In December 1953, the patient was readmitted for elective resection of the proximal jejunum (Mr Stewart) The duodenojejunal flexure was mobilised and about 40 cm of the ulcer bearing proximal jejunum was resected with end to end duodenojejunal anastomosis With a more distal loop of jejunum a classical Polya subtotal gastrectomy was then done (fig 5A and B) The postoperative course was uncomplicated

*Sixth Admission and Fourth and Fifth Laparotomies*—In January, 1954, two days after discharge, the patient returned complaining of severe upper abdominal pain She was febrile, with a white cell count of 17,000 per c mm An indefinable mass was felt in the left upper abdominal quadrant, and an intraperitoneal collection of pus was diagnosed Before exploration could be contemplated two further hæmatemeses occurred At gastroscopy the stoma was well visualised, but no ulcer was seen The volume of aspirated fasting gastric juice was 70 ml containing 24 units of free HCl

At exploration it was seen that perforation of another ulcer, about 1 5 cm in diameter and situated 2 cm distal to the stoma of the gastrojejunostomy, in the efferent loop, had led to the formation of a large abscess walled off by coils of intestine and omentum To oversew this ulcer was technically impossible, the most that could be done was to plug it with omentum The gastrojejunostomy was unpicked and the jejunum repaired The remainder of the stomach was excised and a loop of jejunum well distal to the ulcer was anastomosed to the œsophagus, with side to side jejunojejunostomy (fig 5C)



Fi sites of jejunal ulcers B, anatomical result following jejun with duodenojejunostomy and subtotal gastrectomy C, tomical result (total gastrectomy) X site of postoperative and perforation

The postoperative course was stormy, with paralytic ileus and bilateral pleural effusion as complications After two weeks a mounting temperature and white cell count, with a palpable mass in the left loin, indicated a further collection of pus Exploration revealed a large left-sided retroperitoneal abscess which was drained The patient made an uninterrupted recovery

*Pathology*—The specimen obtained at the time of subtotal gastrectomy consisted of 40 cm of proximal jejunum, including its mesentery, which contained several enlarged lymph nodes The lumen of the jejunum was narrowed to the diameter of a lead pencil opposite the site of the ulcer, which had previously been oversewn Six ulcers, varying in diameter from 0 5 to 1 5 cm, scattered haphazardly round the circumference of the bowel, were present in the proximal 20 cm of the jejunum Both macroscopically and microscopically (fig 6) the ulcers had the appearances of peptic ulcers of other sites The surrounding jejunal mucosa was normal Heterotopic gastric mucosa was not present in serial sections Chronic inflammation alone seen in the mesenteric lymph nodes

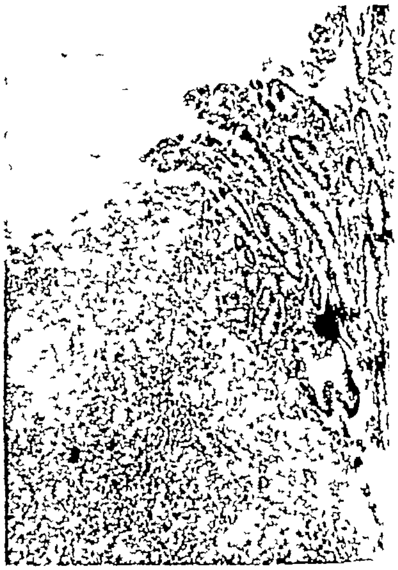


Fig 6—Section of edge of one of six ulcers resected portion of proximal jejunum Part sloughing fibrinous base is in left-hand of field

## Discussion

At the time of Ebeling's (1933) review the mortality rate from primary jejunal ulceration with perforation was 68 5% Notwithstanding subsequent improvements in surgical and related techniques the patient is indeed fortunate in having survived so many hazardous complications

The distribution by age and sex of primary jejunal ulceration is strikingly similar to that of duodenal ulcer Among those affected the ratio of males to females 3 5 to 1, and symptoms and complications usually occur in the fourth, fifth, and sixth decades of life The range of age distribution, however, is great, a child aged years being the youngest patient recorded (Kirmisson 1898) and a man aged 77 the oldest (Velter 1924) So far as can be ascertained, our patient is the youngest female on record

The repeated inability to demonstrate a lesion either radiologically or gastroscopically to explain the obvious symptoms of peptic ulceration was a source of perplexity for two years In retrospect, the constantly seen dilatation of the duodenum and the absence of peristalsis in the jejunum in barium studies was of diagnostic significance Even if ulcers in the jejunum are not radiologically demonstrable, it seems that a diagnosis can be tentatively made, before dangerous complications develop, on t basis of a history of ulcer pain and the radiological demonstration of abnormalities of muscular tone in he duodenum and jejunum A study of radiological findings in previously reported cases supports this view

The nearer the ulcers lie to the duodenojejunal flexure he closer do the symptoms simulate those of duodenal ulcer The periodicity of pain, its relation to meals and he relief obtained from acid neutralising agents were all characteristic of duodenal ulcer pain and suggest a similar mode of origin (Bonney and Pickering 1946) Later the component of abdominal colic was added to the underlying dyspeptic pattern suggesting abnormal peristaltic activity proximal to the sites of ulceration As in more proximal peptic ulcers bleeding was invariably followed by temporary relief of pain

Of the various complications common to all peptic ulcers perforation has occurred in about 80% of all cases of primary jejunal ulceration In a large number of cases it has been the mode of presentation Preceding trauma has often been implicated indeed with deep seated ulceration of so thin walled a viscus it is not surprising that sudden alteration of intra abdominal tension may be a precipitating influence In a case of medicolegal interest the *British Medical Journal* (1906) reported that a jejunal ulcer was fatally perforated by a blow on the abdomen

The occasion afforded the coroner the opportunity of pillorying a member of the (medical) profession and various newspapers some striking headlines.

Recurrent hæmatemesis and melæna the outstanding diagnostic problem of our case are much less common we know of only 2 published cases (Schmilinski 1910 Murphy 1916) Stenosis of the jejunum has been described by Ebeling (1933)

We have consistently referred to primary jejunal ulcers as peptic ulcers for on clinical and pathological grounds there seems very good reason to do so Histologically their appearances are indistinguishable from hose complicating gastro enterostomy and from chronic gastric and duodenal ulcers indeed 2 cases have been published of the association of primary jejunal ulcers with ulcers in more proximal sites with chronic gastric ulcer (Barber 1926) and with duodenal ulcer (Murphy 1916)

The quite phenomenally high level of acid secretion in his patient was of obvious ætiological importance Even conventional subtotal gastrectomy failed to reduce otal acid secretion sufficiently to prevent the development of further jejunal ulceration Although pH gradients were regrettably not studied it is reasonable to assume that even in the presence of normal pancreatic and bile secretion the pH of jejunal contents during interdigestive phases was considerably lower than normal The susceptibility of jejunal mucosa to acid peptic ulceration is well known What is of great interest s the negative observation that in the presence of such an abnormal degree of hyperchlorhydria the patient did *not* have a duodenal ulcer In the genesis of duodenal ulcer it is clear that two factors are involved: the level of gastric acidity and factor X the inherent susceptibility to ulceration of the duodenal mucosa The elucidation of factor X which may be due to local reflex ischæmia or to a defect in the local mucous protecting barrier Hollander 1954) remains one of the most outstanding problems in the study of peptic ulcer

After having been a surgical curiosity it is possible hat the patient will eventually provide a hæmatological case report for the total removal of the stomach and a large part of the jejunum in a female so young is almost bound to lead to deficient absorption of both iron and vitamin $B_{12}$ From the point of view of deficient absorption of iron it is perhaps fortunate that owing to hypo ovarian function she has no menstrual blood loss

## Summary and Conclusions

The case is reported of a young woman who presented with symptoms of ulcer pain and in two years had at least five severe episodes of melæna due to primary ulceration of the jejunum The diagnosis was made at laparotomy undertaken for perforation of the bowel When recurrence of ulceration with further perforation and hæmatemesis followed subtotal gastrectomy, it was considered necessary to remove the remainder of the stomach

Primary jejunal ulceration must be considered in patients with a history of ulcer pain whose stomach and duodenum appear normal on barium meal radiography Suggestive radiological signs are dilatation of the distal duodenum and jejunum with diminished peristaltic activity

Perforation has been a common and hazardous complication of primary jejunal ulceration

Treatment consists in excision of the affected jejunum If preoperative studies reveal normal secretion of gastric HCl subtotal gastrectomy in addition will probably suffice but if severe hyperchlorhydria is present total gastrectomy must be considered

We are extremely grateful to Mr Hector Stewart and Dr Gerald Moss for permission to cite records of the case whilst she was under their care and Mr R Van Raalte for the photographs

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# PROLONGED ANURIA TREATED BY INFUSION INTO THE VENA CAVA

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The management of prolonged anuria by continuous infusion into the vena cava was recently described by Russell et al (1954) The following case further illustrates the use of this method in conjunction with biochemical control of electrolytes

## Clinical Record

Mrs S aged 44 was admitted to hospital on April 19 1954 for repair of a prolapse A Manchester operation was carried out on April 21 but because the patient was anæmic she was given an intravenous transfusion of one pint of group O rhesus negative blood before operation During the operation there was considerable bleeding and it was decided to continue the transfusion Blood had previously been cross matched for her and was held in the hospital laboratory but through an error the blood which was sent to the operating theatre was for another patient of similar name who was also for operation that afternoon This blood was group A rhesus p and the mistake was unfortunately not discov 300 ml had been administered

*Management*

Twelve hours later the patient had secreted only 1 oz. of urine, so the Bull régime of dextrose and peanut oil by intragastric drip was begun (Bull et al 1949) During the next eight days the urinary output remained very low, as little as ½ oz being collected in twenty four hours (fig 1) Vomiting was troublesome from the second day, and on April 29, when her blood urea had reached 361 mg per 100 ml , she began to have profuse diarrhœa 23 oz of fluid was lost from the bowel on April 29, 85 oz on the following day, and 24 oz on the morning of May 1

The timely appearance on this very day of the paper by Russell et al (1954) prompted us to revise our plan of treatment The patient was becoming extremely dehydrated and the alimentary tract apparently no longer afforded a satisfactory avenue for hydration and nutrition Since further diarrhœa would probably have led to extreme dehydration and death, at midday on May 1 the Bull régime was discontinued and an infusion was begun through a ' Polythene ' catheter passed up the saphenous and femoral veins of the right thigh into the vena cava This was maintained for eleven days, and during this time the urinary output rose steadily to 107 oz on May 11, when the infusion was continued We had intended to leave it longer, but the of a sacral bedsore made this impracticable

The constitution of the infusion (see table) was daily to give an adequate fluid intake, to maintain a reas alkali reserve, to ensure a sufficient calorie intake, achieve a balance of sodium and potassium To thrombophlebitis, 15,000 units of heparin was to the 40% glucose solution Heparin was not added less concentrated solutions Estimations of the time were made to ensure that the dosage was not exc Vitamins in the form of ' Becosym ' (Roche) 1 ampoule ascorbic acid 100 mg , were given daily by intramus injection from May 3 until the patient returned to fu

*Progress*

From May 11 the patient was given fluids by mouth, on May 14 light diet was begun Although the urinary continued to increase—indeed it reached a figure of on May 28—the concentrating power of the kidney this period remained seriously impaired, and the urea-c was therefore considerably diminished (fig 1) This

BIOCHEMISTRY OF BLOOD, URINE, FÆCES, AND VOMIT (FROM START OF INFUSION INTO VENA CAVA), AND FL GIVEN BY INFUSION AND BY MOUTH

| Date (May) | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Days from onset of anuria | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 |
| *Blood* | | | | | | | | | | | | | | |
| $CO_2$ combining power (%) | 23 6 | 40 8 | 33 8 | 39 5 | 40 4 | 49 0 | 41 0 | 47 0 | 59 5 | 46 2 | 55 1 | 56 0 | 48 1 | 40 4 |
| $HCO_3$ (*m eq per litre*) | *10 6* | *21 1* | *15 2* | *17 6* | *18 0* | *21 9* | *18 4* | *21 0* | *26 5* | *20 8* | *24 6* | *25 0* | *21 6* | *18 0* |
| Chloride (mg per 100 ml ) | 324 | 310 | 300 | 295 | 285 | 275 | 327 | 330 | 354 | 342 | 376 | 385 | 390 | 400 |
| (*m eq per litre*) | *91* | *87* | *85* | *83* | *81* | *78* | *92* | *93* | *100* | *97* | *106* | *108* | *110* | *113* |
| Sodium (mg per 100 ml ) | 340 | 296 | 290 | 360 | 290 | 290 | 300 | 335 | 330 | 310 | 325 | 340 | 305 | 300 |
| (*m eq per litre*) | *149* | *130* | *127* | *157* | *127* | *127* | *132* | *146* | *144* | *135* | *142* | *149* | *133* | 132 |
| Potassium (mg per 100 ml ) | 27 0 | 18 4 | 22 6 | 20 2 | 20 2 | 27 2 | 23 0 | 18 0 | 17 6 | 16 8 | 16 8 | 17 2 | 16 8 | 21·6 |
| (*m.eq per litre*) | *7 1* | *4 7* | *5 8* | *5 2* | *5 2* | *7 0* | *5 9* | *4 6* | *4 5* | *4 3* | *4 3* | *4 4* | *4 3* | *5 5* |
| Hæmoglobin (g per 100 ml ) | | 14 9 | 9 1 | 9 3 | 12 1 | 10 0 | 9 7 | 10 0 | 9 7 | 9 1 | 8 8 | 10 7 | 9 4 | 10 4 |
| (% *Haden*) | | *96* | *54* | *59* | *77* | *64* | *62* | *64* | *62* | *58* | *56* | *68* | *60* | *66* |
| Plasma proteins (g per 100 ml.) | | | | | | | | | | | | | | |
| Total | | | | | 6 0 | 6 1 | 6 8 | 6 40 | 6 5 | 6 5 | 6 8 | 7 2 | 7 54 | 7 2 |
| Albumin | | | | | 2 1 | 2 3 | 2 5 | 2 76 | 2 8 | 2 5 | 2 3 | 2 7 | 2 66 | 2 7 |
| Globulin | | | | | 3 9 | 3 8 | 4 3 | 3 64 | 3 7 | 4 0 | 4 5 | 4 5 | 4 88 | 4 5 |
| Urea (mg per 100 ml ) | 396 | 440 | 392 | 406 | 432 | 456 | 340 | 396 | 410 | 202 | 252 | 280 | 240 | 228 |
| *Urine* | | | | | | | | | | | | | | |
| Vol per 24 hr (ml ) | | 138* | 280 | 450 | 620 | 720 | 1260 | 1700 | 2540 | 3000 | 1310 | 1905 | 2010 | 1380 |
| Specific gravity | | 1 012 | 1 008 | 1·008 | 1 008 | 1 008 | 1 008 | 1 007 | 1 009 | 1 012 | 1 010 | 1 009 | 1 008 | 1 010 |
| Urea (g per 100 ml ) | | | | 0 95 | 0 95 | 0 86 | 0 90 | 0 91 | 0 91 | 0 90 | 0 92 | 0 91 | 1 12 | 1 00 |
| (g eliminated in 24 hr ) | | | | 4 3 | 6 0 | 6 3 | 11 3 | 15 5 | 23 0 | 27 0 | 12 0 | 17 2 | 22 5 | 13 8 |
| Salt loss (as NaCl) (g per 24 hr ) | | 0 37 | 0 44 | 1 62 | 2 3 | 2 8 | 4 6 | 6 8 | 10 2 | 12 6 | 5 5 | 6 9 | 7 2 | 4 1 |
| Sodium loss (g per 24 hr ) | | | 0 35 | 1 8 | | 1 4 | 3 8 | 2 5 | 7 7 | 8 2 | 2 3 | 4 9 | 3 2 | 2 1 |
| Potassium loss (g per 24 hr ) | | 0 36 | 0 25 | | 0 46 | 0 62 | 1 0 | 1 4 | 2 2 | 2 0 | 1 1 | 2 4 | 2 1 | 1 9 |
| *Vomit* (V) *and Fæces* (F) | | | | | | | | | | | | | | |
| Vol per 24 hr (ml ) | Nil | 95 (V) | 20 (V) | Nil | Nil | Nil | 35 (V) | Nil | Nil | Nil | 670(VF) | 620 (V) | 40 (V) | 375 (V) |
| Salt loss (as NaCl) (g per 24 hr ) | | 0 17 | 0 1 | | | | 0 3 | | | | 2 6 | 4 6 | | 2 7 |
| Sodium loss (g per 24 hr ) | | | | | | | | | | | | 0 8 | | 0 5 |
| Potassium loss (g per 24 hr ) | | | | | | | | | | | | 1 0 | | 0 6 |
| *Fluids by infusion into vena cava* (*oz*) | | | | | | | | | | | | | | |
| Dextrose (40 %) | 20 | 20 | 40 | 20 | 40 | 20 | 15 | 40 | 40 | | ‡ | | | |
| Sodium lactate (in water) | 40 | 20 | 20 | 20 | | | | | | | | | | |
| (in normal saline) | | | | | 40 | | | | | | | | | |
| Sodium citrate (3 8 %) | | | | | | | 10 | | | | | | | |
| Dextrose (5 %) (in water) | 60 | | | | | | 30 | 10 | 10 | | | | | |
| (in saline) | | | | | | 40 | | 60 | 60 | 10 | | | | |
| Normal saline | | | | | | 10 | 20 | | | | | | | |
| Blood | | | | | 20 § | | | | | 40 | | | | 40 § |
| *Fluids by mouth* (*oz*) | | | | | | | | | | | | | | |
| Water | 12 | 15½ | 13 | 2½ | Nil | 2 | | | | | | | 2 | |
| Lucozade | | | | | | | 5 | 14 | 52 | 20 | | | | |
| Milk | | | | | | | | | | 20 | 20 | | | 50 |
| Special mixture¶ | | | | | | | | | | 80 | 70 | 30 | 104 | 65 |
| Other beverages (tea fruit-juice &c ) | | | | | | | | | | | 30 | 35 | 3 | 5 |

* Catheter specimen

† No further vomits occurred before patient s discharge except for 166 ml on 25th day Only liquid fæces suggesting onset of d were collected for analysis Small solid stools were disregarded

‡ Catheter removed

§ Packed cells

pheral vein

mixture consisted of M/6 sodium lactate (4 fl oz ) potassium chloride (gr 7½), sodium chloride (gr 22½ ) lactose (gr with fruit juice (10 fl oz )

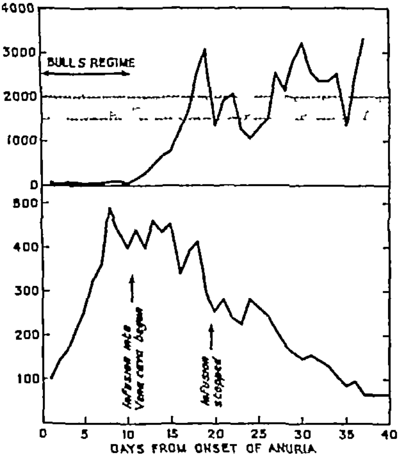

Fig 1—Relationship between urinary output and blood-urea.

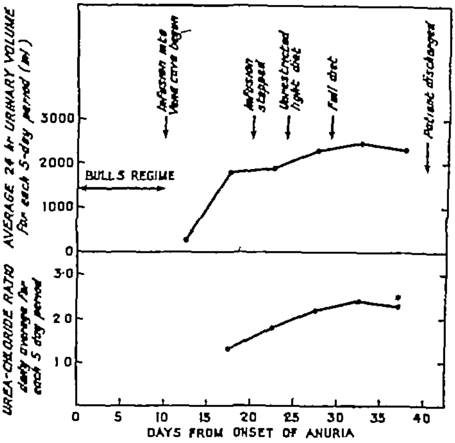

Fig 2—Rise in the urea-chloride ratio which accompanied the increased output. Three-day average ratio

oved however and with the administration of adequate the blood urea level gradually fell, and on the patient s arge from hospital on June 2 it was only 67 mg per ml Three weeks later it had fallen to 51 mg per 100 ml he urea-clearance remained only 36% of normal A month the blood urea was 42 mg per 100 ml and the urea ance had risen to 48% of normal The most recent test ed out on Sept 29 (162 days after the onset of the anuria) ed a blood urea of 35 mg per 100 ml and a urea-clearance of normal Further improvement in the renal function is dently expected

e patient's gynæcological condition remained satisfactory ghout, and the repair of the prolapse appears to have been ssful The patient s general condition is now good and ally she appears normal

BIOCHEMICAL INVESTIGATIONS

*ytical Methods*

ood urea was estimated by the colorimetric micro method ober and Robb described by King (1951) urinary urea ho hypobromite method Serum proteins were estimated he biuret method of Wolfson et al. (1948) Plasma ide was estimated either by the method described by (1951) or direct in the plasma without deproteinisation he rapid method of Schales and Schales (1941); direct tion with silver nitrate using potassium chromate ator was employed for its estimation in urine vomit and s. Sodium and potassium were estimated throughout on EL flame photometer Carbon-dioxide combining power determined by the Van Slyke method

*lts*

or the first nine days of treatment before the start of the sion into the vena cava only the blood urea was estimated its level rose steeply as the period of anuria lengthened 1) From the tenth day of anuria when the infusion the vena cava was begun detailed analyses were made lood urine vomit and of the one specimen of liquid s passed (see table) The blood constituents mentioned o were estimated daily until the twenty third day—i.e *s days after the intracaval infusion was stopped By then* blood urea level had dropped to approximately half its value and the over all biochemical picture was much e satisfactory Clinically the patient was improving but her veins had suffered from the repeated vene tures It was therefore decided to discontinue the daily d-chemistry investigations except for blood-urea and oglobin estimations which could be done on samples ined by finger prick A final complete examination was ied out on the twenty-eighth day

he urine was examined daily for twenty four hour volume specific gravity Chlorides sodium, and potassium were estimated with a view to making good the daily loss of these constituents; and the daily output of urea was also determined These procedures were also continued until the time of the patient s discharge The results obtained from analysis of urine vomit and liquid stool for the thirteen days of detailed investigation following the setting up of the infusion into the vena cava are set out in the table, below the corresponding results obtained from blood analysis.

The daily urine volumes up to the time of the patient s discharge, together with the values for blood urea are shown in fig 1 The diuresis which rapidly followed the start of the infusion was accompanied by a significant drop in the blood urea level Although subject to rather large daily fluctuations, the flow of urine continued to be satisfactory after the polythene catheter was removed and oral fluids were begun The blood urea, which was 440 mg per 100 ml immediately after insertion of the catheter had fallen to 252 mg at the time of its removal and to 63 mg at the time of the patient s discharge

The urine was of low specific gravity throughout (1 003-1·012) The usual value was 1·006–1 009 and varied approximately in inverse relation to the volume The urea concentration was consistently low and varied with the specific gravity The highest value recorded was 1 12 mg per 100 ml (usually it lay between 0 7 and 0 9 mg per 100 ml); which suggests that during the initial period of renal recovery the concentrating power of the kidney was poor and elimination of urea was effected mainly by an increase in the urinary volume A large urinary output was encouraged by allowing the patient who was very thirsty to drink fluids ad lib Muirhead et al (1948) in their study of a series of similar cases, showed that an increase in the urea/chloride ratio took place concurrently with recovery and they suggested that this might be of prognostic value The urea chloride ratio was therefore determined daily and was found to rise steadily—a point brought out more clearly when the five-day averages were plotted (fig 2) The rise is proportionate to the increase in the average twenty four hour urinary volume for each five-day period

## Discussion

This case demonstrates firstly how very easy it is despite routine precautions to give an incompatible blood transfusion to an unconscious patient To prevent a recurrence of this, blood is now issued from our hospital laboratory only on receipt of a written requisition bearing the patient s full name age and registration number Only the timely appearance of the paper by Professor Russell and his colleagues enabled us to avoid a fatal outcome since the copious diarrhœa made the Bull regime ineffective At the start of the extensive biochemical investigations one of the most dangerous features of this case was severe acidosis The infusion into the vena cava enabled prompt rectification of the acidosis with $M/6$ sodium lactate, as well as rapid correction of dehydration resulting from the diarrhœa, which would not have been possible with a peripheral venous infusion

In the management of this case several minor points arose which are worth mentioning

(1) It is inadvisable to use the intravenous catheter to obtain samples of blood for analysis since the procedure may disturb it as well as increase the risk of sepsis It may, however be used to obtain essential samples of blood if no peripheral vein is available

(2) Prophylactic procaine penicillin (1,000,000 *units daily*) was begun on May 1 but was discontinued after three days because an urticarial rash developed In spite of daily bladder lavage, the urine subsequently became infected with *Staphylococcus pyogenes*, but the infection was successfully treated with a course of erythromycin

(3) In order to prevent displacement of the catheter it was necessary to limit the patient's movements, which resulted in the development of a bed sore This healed rapidly with routine treatment once the catheter had been removed and the patient's mobility restored

(4) In view of the risks attendant upon intravenous potassium therapy, a low serum potassium level was disregarded until potassium chloride could be administered cautiously by mouth

(5) When the time came to start feeding the patient orally, lactose was chosen in preference to glucose, since it is less sickly and therefore less likely to cause vom
at that stage, might have been dangerous

## Summary

A case of prolonged anuria due to incomp
transfusion is recorded

After ten days on the Bull intragastric
diarrhœa supervened of such severity as to r
treatment by this method ineffective

Infusion into the vena cava was substit
next ten days, and this made possible ex
chemical control of fluids and electrolytes u
began

By using a 40% glucose solution in the inf
possible to supply sufficient calories in a m
volume of fluid

—We are indebted to Dr Patrick Kidd for his
advice, to Dr C J Thornberry, Dr D B
H F Juckes, and Sister M Curtis for their dev
the management of this case, and to Mrs P
B F Savage, and Mr G C Ross for their skil
assistance Mr F V Hughes constructed the fig

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*clin Path* 18, 723

# Medical Societies

## ROYAL SOCIETY OF MEDICINE

### Anæmia in General Practice

THE section of general practice met on Dec 15, with Dr R J Minnitt, the president, in the chair, to discuss the Management of Anæmia in General Practice

Dr Douglas French described the incidence of different types of anæmia in his practice of some 5000 patients Patients with iron deficiency anæmia averaged 80 a year, half of these cases were associated with pregnancy In eleven years he had seen only 13 patients with pernicious anæmia, 2 with chronic myeloid leukæmia, 1 with acute leukæmia, and altogether 10 with the rare types of blood-diseases, he had 4 hæmophiliacs in his practice, 3 of them in one family These figures meant that, judging by his experience the general practitioner had to deal almost exclusively with iron deficiency anæmia, other types were relatively rare and needed hospital investigation for proper diagnosis It followed that vitamin $B_{12}$, folic acid, liver extracts, or mixtures containing these substances were rarely needed, and they should in fact never be used unless there was a clear therapeutic indication for them Dr French did blood counts—red cells, hæmoglobin, white cells (total and differential)—on all anæmic patients Anæmia was rarely very urgent, and it paid to spend a few days on correct diagnosis rather than start treatment which might prove after some weeks to be incorrect The colour index was a useful guide to sorting cases, if it is over 1 0, the patient should be sent to hospital and no treatment should be given If the colour index was about 1 0 iron deficiency anæmia was the most likely diagnosis, so treatment with iron was given, but the patient was sent to hospital if the response was not up to expectations It was important to regard iron deficiency as a physical sign, not as a diagnosis per se a cause for the anæmia must be sought —in particular, tuberculosis peptic ulcer, complications of pregnancy malignant disease rheumatoid arthritis, and bleeding hæmorrhoids must be considered

In treating the anæmia, "an air of expectant scepticism" be maintained, and one should be careful not to spoil clues for subsequent specialist examinat
should be needed Oral iron should give a
rise of 1% (0 148 g per 100 ml) per day
difference was found between inorganic sal
ferrous sulphate, and organic salts, such
succinate Intravenous iron gave a rather
rise, and Dr French used this preparation
patients with an initial hæmoglobin of less
(9 g per 100 ml), (2) all patients with h
anæmias of pregnancy, (3) the minority of p
genuinely failed to respond to oral iron,
cases in which the diagnosis was in doubt
injections were given daily if possible, since t
patient interested, and the course was quickly
The dose used was 25 mg Fe per 1% hæmoglo
and this sufficed, he found, to give a reticulo
8–10% on the fifth to eighth day If intra
did not restore the blood picture to norm
important to look for chronic blood loss an
diseases already mentioned

In pregnancy the presence of hydræmi
remembered, Dr French suggested from
observations that a red cell count of 4,000,00
and hæmoglobin of 80% (12 g per 100 r
twentieth week was normal He pointed out th
a physiological rise of hæmoglobin on the da
a fall on the first three days of the puerperium,
gradual recovery to normal levels in the next
these normal variations tended to be forg
assessing the value of iron preparations in
anæmia In the true iron deficiency anæmia of
intravenous iron was the most effective treat

Dr M C G Israëls agreed that the c
provided a useful guide to the practitioner's
action and he pointed out that almost all t
whose anæmia was not due to iron deficiency
least outpatient hospital investigation for pr
ential diagnosis A colour index about 1
malignancy (especially of the alimentary tra
loses (including Hodgkin's disease), or ur
some of these patients proved to have pri
deficiency anæmia A colour index over 1
quite a different group of diseases pernicio

ukæmia (especially the aleukæmic forms), acquired æmolytic anæmia sprue and non tropical steatorrhœa nd aplastic anæmia Dr Israëls dealt with the differ ntial diagnosis of these conditions and pointed out how uportant it was *not* to give vitamin $B_{12}$ folic acid or ver or any of the so called complete hæmatinics to hese patients before the diagnosis was settled since hese substances were liable to confuse the diagnostically ritical examination of the bone marrow He emphasised hat the various hyperchromic anæmias all needed quite ifferent treatment

In pregnancy the physiological hydræmia meant that eliance could not be placed on the colour index which ught often be over 1 0 without there being a megalo lastic change in the marrow The diagnosis of megalo lastic anæmia of pregnancy could be settled only by one marrow examination and this should certainly be one for every patient whose hæmoglobin level was elow 9 g per 100 ml (70%) and who did not respond o parenteral iron If megaloblastic changes were found reatment with folic acid soon restored the blood picture

Dr CHARLOTTE NAISH asked about anæmia in old ersons which changed from hypochromic to hyper hromic with iron treatment given liver they improved Vas not this a case for the use of the condemned 'blunderbusses'? The answer was definitely No he type of hyperchromic anæmia should be established irst and Dr Israëls drew her attention to the fact that folic acid must not be given to patients with pernicious anæmia

Dr JOHN HUNT said that blood-counting was time consuming for the general practitioner would not a hæmoglobin estimation be enough? Dr FRENCH thought that if the hæmoglobin was less than 85% the red cells should be counted

Dr R M S MCCONAGHEY remarked that it was very important to impress on patients with iron deficiency anæmia that the treatment had to continue for two to three weeks before the patient felt really improved otherwise the patient was liable to become discouraged and stop treatment too soon

Dr J N M CHALMERS mentioned the new intramuscular iron preparations and said that in one case he had seen a rise in hæmoglobin from 35 to 90% with three weeks treatment during which 53 ml of 'Imferon' was given This material gave rise to local discomfort rather more commonly than some reports suggested

Other speakers pointed out that Dr French used a lot of intravenous iron was it really necessary to use it so often in preference to oral iron? Dr FRENCH agreed that it was not really necessary Most patients could tolerate one or other of the many oral iron preparations He had been working on the effects of these intravenous preparations, and they did have the advantage that the doctor could be sure that the patient had received a proper dose

# Reviews of Books

## Clinical Psychiatry

W MAYER-GROSS M.D Heidelberg, F.R C.P director of clinical research, Crichton Royal Mental Hospital Dumfries; ELIOT SLATER M.A M D Camb., F R C.P D P M physician in psychological medicine The National Hospital London MARTIN ROTH M D Lond. M.R.C.P director of clinical research Graylingwell Hospital Chichester London Cassell 1954 Pp 652 50s

THIS is the most considerable textbook on psychiatry et published, or likely to be published for some time, in nglish Its bibliography is far more extensive and international than is usual The legal aspects of psychiatry re reviewed as they affect not only Britain and America ut also France, Germany Scandinavia and other ountries. Mental defect is discussed early affording clear introduction to those many conditions where sychiatric syndromes direct attention to a more primary isorder whether toxic, inflammatory handicapping primarily psychotic In describing the gross or minute ructural lesions which may first present as mental isorder the authors combine sound pathology with spect for psychiatric observation The sections on the pilepsies and cerebral trauma are written in a highly imulating manner and the critical assessment of ucotomy as a treatment for schizophrenic disorders hould convince many that modern psychiatrists are ell aware of both the losses and the gains achieved hrough recent advances in treatment Some will regret hat the descriptions of psychopathic states and neurotic ersonalities have been combined in one large chapter much that these authors write of the history of odern concepts is good that clearer views on the ature of psychopathic states might have been expected them But the chapter as a whole contains many uminating passages the unstable drifter the vagrant id the sexually abnormal are all well described encies is more fully dealt with than usual The authors aim—and back their view with statistics—that the sults of analyses of large groups of patients yield ore trustworthy evidence on the causes of mental sorder than does psycho analysis by Meyerian or reudian methods of small numbers It seems likely hat most criticism of the book will be concerned with is claim Dr Mayer Gross and his colleagues have llowed good precedent in collecting collating and nalysing an abundance of data and much support is fered for their deductions. Psychotherapists who wish to refute these must face the challenge of their carefully collected case-material Some will hope that the authors determinism will be modified by the accumulation of yet more facts

## Chemical Pathways of Metabolism

Vol. II Editor: DAVID M GREENBERG department of physiological chemistry University of California New York: Academic Press 1954 Pp 383 $9.50

THE second volume which completes this treatise follows hard on the first.[1] This time the contributions are all from laboratories in the United States. The first five deal with amino-acid metabolism, and the others are on the purines and pyrimidines, the nucleotides and nucleosides and heme and chlorophyll. They are clearly written with enough structural formulæ to make them easy to follow Those who have not been closely associated with this kind of work will be amazed at the way in which our knowledge of all this intermediary metabolism has been enhanced by the use of radioactive isotopes. How could we ever have found out without them that the C atom lying between the two atoms of nitrogen is derived from formate in the purines but from $CO_2$ in the pyrimidines?

## The Brompton Hospital

*The Story of a Great Adventure* MAURICE DAVIDSON M.A D M Oxfd, F.R C P consulting physician to Brompton Hospital F G ROUVRAY O B E., late house governor Brompton Hospital. London Lloyd Luke, 1954 Pp 152 21s

Brompton Hospital owes its inception to Philip Rose, a solicitor He was impressed by the facts that consumption was the most common and fatal disease destroying a third of the population yet the doors of all hospitals were closed against it His attention had been drawn to the problem when he was unable to obtain hospital treatment for a consumptive clerk employed by his firm

The hospital opened in the Manor House near the Royal Hospital Chelsea on Sept 13 1842 There was accommodation for 20 patients and it is hardly surprising to learn that this was nothing like enough An extension of the house was found to be impracticable and the committee accordingly decided on the more ambitious scheme of erecting a new building to accommodate by successive additions 100 to 200 inpatients The site chosen was at Brompton "a village in Kensington, remarkable for the salubrity of its air and surrounded entirely by nurseries and garden grounds which were amongst the first cultivated in the country " The ground was formerly part of a botanical garden The new building came into use in 1846 and since then the hospital has gone from strength to strength The new wards were ventilated by a forced supply of warmed air, which was held to provide " for the poor a climate nearly approaching that of southern latitudes, the advantages of which can only be enjoyed by the more favoured portion of the community "

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[1] See *Lancet* 1954 ii 964 1110

There are short biographies of the doctors who have done so much to gain for the hospital its great international reputation—among them Richard Quain, Burdon Sanderson, Douglas Powell, Kingston Fowler, and Percy Kidd The book is intended for lay readers and it will appeal to them, but it will appeal most to those who are proud to have been associated with " Brompton "

### The Biochemistry of Semen

T Mann, M.D , SC D , PH D , F.R S , reader in physiology of animal reproduction, University of Cambridge London Methuen. New York John Wiley 1954 Pp 240 16*s*

As Dr Mann points out in his preface, information on the physiology of semen, and particularly its chemical aspects, is scattered among books and journals, many of which are inaccessible Lack of a comprehensive and up-to-date treatise has handicapped the now numerous biochemists, clinicians, zoologists, and veterinarians concerned with this subject Dr Mann has himself made many important contributions to semen chemistry and physiology since he became especially interested in this subject in 1944, and in this scholarly book he condenses an immense amount of information into a relatively small space The bibliography alone includes nearly a thousand items

He begins with a synopsis of the principal structural and physiological features of spermatozoa and the accessory glands There is a detailed account of the physical and chemical properties of semen—many mammalian, as well as non mammalian species receiving due consideration—and of the methods used for the evaluation of semen quali Next, the influence of extraneous factors—such as hormo sperm egg interacting substances, spermicidal agents, se dilutors, ionising radiation, and deep freezing—is describ Other chapters deal with metabolic processes which sup the spermatozoa with energy for their motility and surviv and special attention is given to seminal fructose (the s which Dr Mann has made peculiarly his own), the occurre of inositol, lipids, citric acid, and nitrogenous bases includ spermine, choline, and ergothioneine, and the pr constituents and enzymes of spermatozoa and se plasma

**Advances in Ophthalmology** (Vol VII–VIII T Hague Uitgeverij Dr W Junk 1954 Pp 758 guilders) —This double volume of *Documenta Ophthalmol* contains the proceedings of the symposium on the re *circulation held in Strasbourg in 1951*, which survey ophth dynomometry in its physiological and clinical implicat The proceedings of a symposium on squint held in 194 by the Dutch Ophthalmological Society while Holland under Nazi occupation are also included Some of the is now out of date, but the account of the *genetic aspects of t* affection by Waardenburg, and the papers on binocular and fusion movement by F P Fischer and J W Wag are both useful The volume also includes monographs Roelofs on optokinetic nystagmus and by Yap Kie Tion experimental keratoplasty

**Heart** (2nd ed Baltimore Williams & Wilkins Londo Baillière, Tindall, & Cox 1954 Pp 680 114*s*) — Aldo Luisada has added two or three short chapters in th new edition of his book and made many changes *to bring t* *text up to date* He continues to classify cardiac *lesions* on anatomical rather than an ætiological basis, a method whic fails to give the correct perspective for such lesions as mit *stenosis* and *constrictive pericarditis* The first chapter those who have made outstanding contributions to cardiol from 1530 to the present day, but no British physicia mentioned after 1912 though two British surgeons are includ The book is well produced on heavy glossy paper, but t price has doubled since the first edition

## New Inventions

### A SMALL URINARY-FISTULA SUCTION-CUP

A URINARY fistula is tedious not only to the patient, whose skin often becomes excoriated, but also to the nurses, who have to keep changing soaked dressings Furthermore large quantities of dressings are required Hamilton Irving introduced his suprapubic apparatus in an attempt to reduce these difficulties, but it was cumbersome and (especially where the patient was obese) it often leaked and caused *pressure sores under* the retaining straps The basic principle of draining the urine into a receptacle without a tube in the fistula was sound, however, and I have therefore used it in designing a suction-cup (fig 1) I describe here This is small and very simple to use and works equally well with little or no attention, whatever the configuration of the patient Being made of ' Perspex ' it should be sterilised by a cold antiseptic solution, and it is fixed over the fistula with strips of ' Elastoplast ' The air inlet is placed uppermost, and the tube, draining from the lowest point, is connected by small-bore pressure-tubing to a Roberts silent suction-pump The patient may [illegible]ept dry both in and out of bed

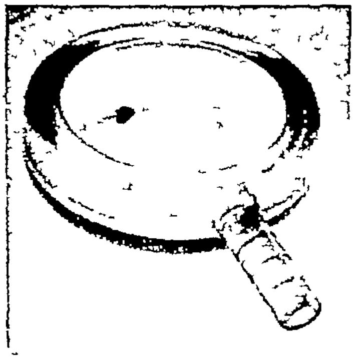

Fig 1

*Although this cup was originally designed for* ur fistulæ it may be used with equal success over fistula draining thin fluid wherever situated Its is adequate for almost every fistula and yet small not to interfere with wound dressings The air inlet (fig 2) allows continuous suction to be used witho creating a partial vacuum and consequent soreness the skin drawn into the cup Furthermore, a curr of air is continuously passing over the skin around fistula, thus preventing it from becoming sodden The inner lip (B) not only prevents urine from seeping between the cup and the skin but also helps the cup to fit more comfortably by increasing the area of contact between the two The connection (C) to which the rubber tube is attached is angled to allow the cup to lie flat even on an obese patient The cup, being made of perspex both light and inexpensive to make

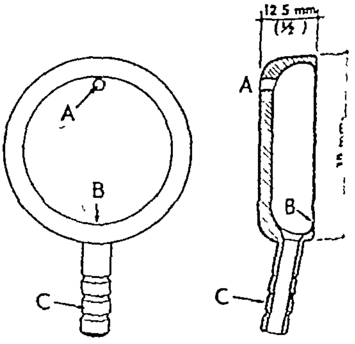

Fig 2.

I am indebted to the Genito Urinary Manufactur Company for making this cup for me from the protot supplied by Mr R A Crispin, to Mr J D Foy for the draw and to Mr F Wardlaw for the photograph This s company also market the Roberts suction pump

Withington Hospital,
Manchester

H F Smith
B SC , M B Manc , F.R C.S

# THE LANCET

*LONDON SATURDAY JAN 8 1955*

## Adrenalectomy for Hypertension

T is more than twenty years since adrenalectomy s first done for the relief of hypertension, and ward of 200 cases treated in this way have now been scribed [1–9] When DeCourcy [2] in 1934 reported favourable effect of partial bilateral adrenalectomy 8 patients with severe hypertension he stated his lief that elevation of the blood pressure was due excessive secretion of adrenaline by the adrenal dulla There is now good evidence that except phaeochromocytoma hypertension is not associated h increased secretion of adrenaline or noradrena e and it is the adrenal cortex that plays the more portant part in pathogenesis Whether its rôle is imary or secondary has been debated at length [10] support of a primary rôle is the clinical evidence at many patients with hyperadrenalism have pertension and that removal of an adrenal cortical imour or total or subtotal resection of bilaterally perplastic glands abolishes the symptoms and signs Cushing s syndrome and often restores the blood essure to normal Conversely hypotension is a ature of Addison s disease Thorn and his associates [9] ve reported that the blood pressure fell to normal in ypertensive patients in whom adrenal insufficiency veloped and in 1 of them hypertension recurred en deoxycortone was given But there is still evidence that essential or renal hypertension is ociated with increased adrenocortical activity with the formation of abnormal adrenocortical rmones and the majority opinion is that adreno-tical hormones have a secondary action which ows other factors to elevate the blood pressure LDBLATT [11] first observed that hypertension induced perimentally by constriction of one renal artery could abolished by adrenalectomy Other workers [12 13] ve shown that in rats adrenalectomy abolishes the pertension which follows nephrectomy in single imals or in animals linked in parabiosis There is no evidence that the adrenal glands maintain this iprival hypertension through their action on ter and salt metabolism [14] because at least in single imals ingested sodium chloride is a partial substitute the adrenocortical hormones

Adrenalectomy is much safer now that it can be lowed by adequate substitution therapy with cortisone (though in some cases deoxycortone is also required) The results are difficult to assess for several reasons Observations on the effects of rest alone [15] of hypotensive drugs,[16] and of sympathectomy [17] have shown that spontaneous variations in the blood pressure may be profound, and that any operation may cause a fall in blood pressure Hence it is difficult to obtain satisfactory controls Furthermore the results of adrenalectomy have been assessed by different criteria—in some instances by the effect on the blood pressure alone in others by the effect on symptoms and signs Nor has the operation been uniform In most cases the patient has undergone subtotal bilateral adrenal resection , and some but not all, of these patients have required postoperative substitution therapy Only a few have undergone total adrenalectomy [9] Understandably there has often been 'surgical polypharmacy —adrenalectomy combined with removal of a diseased kidney or with bilateral sympathectomy In the largest published series [5] Adson type sympathectomy has been combined with total or subtotal adrenalectomy Finally some of the patients have had essential hypertension and others unilateral or bilateral renal disease Since the operation is experimental it has been undertaken mainly where the hypertension has been severe (diastolic pressure greater than 120 mm Hg), the patient has failed to respond to intensive medical treatment and there has been evidence of progressive damage to the heart kidneys brain or—particularly—the eyes Because of the high mortality from operation and short postoperative survival in patients with nitrogen retention any impairment of renal function is now accepted as an absolute contra indication to adrenalectomy

Of the 125 patients operated on by the Philadelphia group [5] about a third had a reduction in blood pressure to 150/100 mm Hg and in a further quarter or so the diastolic pressure after operation did not exceed 110 mm Hg Bowers [1] claims that, in a series of 27 patients operated on all but 1 of the 21 survivors subsequently became normotensive DeCourcy [3] claims similarly good results , but in view of the spontaneous fluctuations in blood pressure it is difficult to assess the result when only isolated readings are given The Boston group,[9] who did total adrenalectomy alone give more detailed blood pressure readings Of 12 patients operated on 9 survived three months or longer , and of these only 2 showed a definite fall in blood pressure Despite a profound fall in pressure some patients have died soon after operation of coronary thrombosis or cerebrovascular accidents On the other hand some patients have been relieved of their symptoms and the eye ground changes have regressed without any significant change in blood pressure—a response that has also been observed after sympathectomy alone One of the most striking changes after adrenalectomy is increased loss of urinary sodium and chloride and in several patients this has led to the disappearance of congestive cardiac failure or pulmonary oedema Although a significant fall in blood pressure late in

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Bowers R I J Amer med Ass 1954 154 391
DeCourcy J L Ann Surg 1934 100 310
DeCourcy J L J int Coll Surg 1950 13 310
Green D M, Nelson J N Dodds G A Smalley R F J Amer med Ass 1950 144 339
Jeffers W A, Zintel H A Hills, A G Hafkenschiel J H, Langfeld, S B Sellers A M Wolferth C C Ann intern Med 1954 41, 421
Pickering G W Wright A D Heptinstall R H Lancet 1952 ii [illegible]
Pickering G W, Heptinstall R H Quart J Med 1953 22 1
Rosenheim M L Brit med J 1954 ii 1181
Thorn G W Merrill J P [illegible] M G Frawley T F Finkenstaedt J T Ann intern Med 1952 37 972
Adrenal Cortex Transactions of the 4th Conference Josiah Macy, Jun Foundation New York 1953 p 131
Goldblatt H, Ann intern Med 1937 11 69
Ledingham J M Clin Sci 1951 10 123
Floyer M A, Ibid p 405
Ledingham J M Ibid 1954 13 335 343

15 Watkin D M, Froeb H F Hatch F T Gutman A B Amer J med 1950 9 441
16 Morrison, B Brit med J 1953 i 1291
17 Evelyn K A Alexander F Cooper S R J Amer med Ass 1949 140 592

convalescence has always been preceded by increased excretion of sodium, loss of this electrolyte is not always accompanied by a decrease in basal blood-pressure ROSENHEIM [8] has reported a case in which there was severe postoperative hypertension despite biochemical findings which indicated advanced adrenal insufficiency Thus the rôle of the adrenocortical hormones and electrolytes in maintaining hypertension remains uncertain In the words of JEFFERS et al [5]

> " This is an experimental approach which cannot at present be recommended as a treatment for hypertension As in the case of sympathectomy, one cannot predict which patients will respond with improvement nor can we discern why certain patients with adequate renal function have failed to improve after operation "

## Peripheral-nerve Injuries

EARLY in the 1939–45 war the Medical Research Council appointed a Nerve Injuries Committee under the chairmanship of the late GEORGE RIDDOCH, and this formed a focal point for the five centres for nerve injuries which were set up as part of the Emergency Medical Service The collaboration of the Services and the Ministry of Pensions ensured that large numbers of patients with serious nerve injuries reached these centres and attended for review for several years after operation Although the staffs at the five centres naturally approached the problem of peripheral-nerve injuries differently, certain standards of thoroughness, methods of examination, and criteria of recovery were followed at each centre, so that experience gained at one could be measured against that at another, to the advantage of both This vein of uniformity has enabled the Nerve Injuries Committee of the M R C to present the combined experience of all centres in a special report [18]

Some fundamental experimental work on the processes of nerve degeneration and repair was being done at Oxford by a team under the stimulating guidance of J Z YOUNG These early studies showed that after a crush injury in which there was degeneration of the axon and myelin sheath the axon tips regenerated at the rate of about 4 mm a day They also showed that, besides the time taken in the axon tips travelling along the " Schwann tubes," there was an initial delay at the site of injury and some delay between the tip of the axon reaching the end-organ and the return of function In laboratory animals this stage of functional recovery was reached at a rate of 2–3 mm a day, and H J SEDDON, P B MEDAWAR, and H SMITH (1943) found that in man likewise the radial nerve regenerated steadily, though at the rather slower rate of 1 5 mm a day RUTH BOWDEN, summarising later work, now shows that the rate of recovery gradually falls off in covering the fairly long distances for nerve regeneration in man, and she points out that the closer the lesion to the spinal cord the faster is the rate of advance But with a high lesion, though the initial progress is faster than with a low one, the outlook is not on that account better

Peripheral nerve injuries give rise to difficult problems in diagnosis and in treatment An excellent illustrated pamphlet, prepared by SIR JAMES LEARMONTH,[19] was widely used during the war and w doubt responsible for many patients being sent nerve injuries centre for fuller investigation. exhaustive clinical examination was supplem by sweating and electrical diagnostic tests, a Edinburgh by a detailed study of the vascular c in nerve injury (described by R L RICHARDS report) The many early difficulties experienc A E RITCHIE and P BAUWENS in electrical dia of nerve injury led to the construction of a apparatus to deliver a " square " wave, the inte and duration of the stimulus being variable Fu rightly suggests that the widely used galvan faradic stimulators for electrical diagnosis shou replaced by a simple stimulator delivering different lengths of shock, of about 1 and 300 m Denervated muscle would require a substantial inc in intensity in changing from the long to the shock, but a normal muscle would not

R B ZACHARY and R ROAF have anal 1500 case-records of lesions in continuity, and lated the clinical and pathological findings in a siderable proportion of these The steps in the dia of a lesion in continuity are (1) distinction bet a degenerative and a non degenerative lesion, (2) subdivision into cases of complete and of inco paralysis, bearing in mind that anomalous inn is common Of 739 cases of complete paralys to open injuries, 621 had complete or partial d of the nerve—a strong indication for explor operation with a view to repair Among c injuries causing complete paralysis, division (c or partial) was very much less common (11 out of Even incomplete paralysis due to partial div is sometimes amenable to repair, and ZACHARY ROAF define those syndromes which are with partial division of the nerve Repair of injuries by direct suture remains the surgeon's contribution Criteria of recovery at all five were similar, and well over 1000 cases of suture which had been followed up for at least years have been analysed by ZACHARY Resul best after suture of the radial nerve; worth improvement ensues in about two-thirds of the Suture of the median nerve is followed by retu sensibility to the tips of the fingers in half the and even with the ulnar nerve some function ret to the interossei in nearly the same prop Improvement after repair of the sciatic nerve often been regarded as so slight that amputation been advised when this nerve is divided Yet th muscle can become strong in at least half the and although there is little sensory recovery m the patients can feel a strong painful stimulus foot Moreover, even with no sensory recovery the foot is by no means useless, provided the and joints are well cared for

One of the most remarkable features of the su of peripheral nerves in the late war was the esta ment of nerve grafting as a reliable measure direct suture was impossible or unlikely to pro a satisfactory result Experimental studies on gr are summarised by F K SANDERS, and SE describes his considerable experience with this

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neral Nerve Injuries Edited by H J SEDDON *Spec Ser med Res Coun Lond* no 282 H M Stationery 1951 Pp 451 55s

[19] Aids to the Investigation of Peripheral Nerve Injuries. War Memorandum No 7 H M Stationery Office 194

ie at Oxford The criterion of success in grafting covery as good as that by direct repair of a small in the same nerve at the same site The most ing successes have been with the median nerve its, using either several strands of a cutaneous ve or a portion of a main trunk—e g , the proximal np of an irreparable ulnar nerve Successful results almost half the cases of nerve grafting is a con rable achievement, and SEDDON's account of this k is a fitting conclusion to this comprehensive ew of British experience in the treatment of pheral nerve injuries in war time

## Raynaud's Phenomenon in Industry

UNDER the Industrial Injuries Act benefit is pro ded for injuries caused by accident arising out of in the course of employment and for certain ases due to the nature of employment Such dis es are prescribed in regulations and are accordingly wn as ' prescribed diseases ' In 1946 the Court Appeal awarded compensation to a workman who med to have developed Raynaud s phenomenon ough the use of a high frequency vibratory tool In ther cases, heard in the Court of Appeal and the use of Lords, the 1946 decision was not wholly tained and in 1949 a tribunal consisting of the lustrial Injuries Commissioner and two deputy com ssioners decided that the incapacity due to Ray ud s phenomenon was not allowable under the lustrial Injuries Act At this stage the Minister of isions and National Insurance asked the Industrial uries Advisory Council to consider whether Ray d s phenomenon should be brought within the by being added to the list of prescribed diseases— s already treated as a prescribed disease in several er countries The inquiry, undertaken by the ustrial diseases subcommittee in the words of the jority report[1] " has been a difficult and protracted "

any investigation into Raynaud s phenomenon ing from long continued use of a vibratory tool is atly handicapped by the lack of data concerning ncidence in various industrial procedures Workers already have dead fingers may be loth to ig it to the doctor s attention, for fear of transfer less well paid job , and from the other side the nagerial staff do not actively invite complaints phenomenon has been described in association h many procedures involving vibratory tools— l-driven polishing, pneumatic drilling shoe pound light riveting hammers, and hand grinding ATE and DRUETT[2] using a piezo-crystal recording nique suggested that the critical frequency range 40–125 cycles per second Many other variables be of equal or greater importance including, for ance amplitude and wave-form of fundamental secondary harmonics strength of grip used, e of material on which the work is done the rator s skill the mechanical efficiency and mass of tool and the operator s susceptibility to the dition Susceptibility varies greatly whereas one ker will complain of Raynaud s phenomenon nin months another under identical conditions may never be troubled A further difficulty is in diagnosis Raynaud's phenomenon due to vibratory tools is unassociated with objective signs other than the colour changes in an attack, and often these are not easily precipitated under laboratory conditions Even if the presence of Raynaud's phenomenon is confirmed how can its association with an industrial process be evaluated ? It has long been recognised that white fingers may develop in a wide range of vascular and systemic diseases, and correct diagnosis may depend not only on detailed clinical and laboratory investigation but also on patient follow up Nevertheless clinicians agree that in the vast majority of cases Raynaud s phenomenon due to a vibratory tool can be diagnosed with reasonable confidence, though the severity of the lesion and the incapacity are more difficult to assess The conclusion of the majority report is that Raynaud s phenomenon rarely interferes greatly with the patient s work But it may affect his leisure hours for gardening, swimming, and other outdoor activities may be impossible for him, and, once established symptoms do not appreciably abate even though the patient abstains from the employment which has given rise to the disorder Having considered all these factors the majority of the subcommittee concluded that any form of prescription of Raynaud s phenomenon would give rise to serious and probably insurmountable practical difficulties especially in deciding individual claims and they advise therefore against its prescription In contrast the minority report which recommends that Raynaud s phenomenon should be a prescribed disease points out that everyone agrees that this condition occurs in industry, and this being so it is the Minister s responsibility to see that competent doctors are made available for diagnosis, as with other prescribed diseases

The situation therefore is still unhappy Possibly a more satisfactory outcome would follow further investigation into the incidence of Raynaud s phenomenon with various industrial procedures involving vibratory tools and the substitution where possible of innocent techniques for those incriminated Such a solution may not be universally feasible, but it could certainly eliminate most of the more harmful occupations

## Heroic Days

> In the natural sciences these are and have been and are most surely likely to continue to be heroic days. Discovery follows discovery, each both raising and answering questions, each ending a long search and each providing the new instrument for new search

NO ONE, perhaps, has a better right to speak of the wonder and terror of our times than J ROBERT OPPENHEIMER, director of the Institute for Advanced Study at Princeton University, formerly a most distinguished adviser of the American government on atomic policy, and now (since the investigation of his character and associations by the Atomic Energy Commission last June) denied all further access to that policy He was speaking, at the celebrations of the 200th anniversary of the founding of Columbia University on the theme chosen for that occasion ' Man s right to knowledge and the free use thereof ALISTAIR COOK in quoting parts of his address in the *Manchester Guardian* of Dec 29, says that OPPENHEIMER narrowed it for his own purposes to "the prospect in the arts and sciences", and within this framework demonstrated a world upheaved A distant survey of the human scene shows what passes for progress

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[1] aynaud s phenomenon Report of the Industrial Injuries Advisory Council Cmd 9347 H.M Stationery Office 1954 p 10 6d

[2] gate J N Druett H A *Brit J industr Med* 1947 4 141

> "that more people are engaged in scientific research than ever before that the Soviet world and the free world are running neck and neck in the training of scientists that the social sciences are pursued actively in America, Scandinavia and England, that there are more people who hear the great music of the past, and more music is composed and more paintings are painted"

But, with more means of communication than ever before, we can speak to each other less The artist, who depends on a common sensibility and culture, on a common meaning of symbols, on a community of experience and common ways of describing and interpreting it, finds himself speaking to air "His audience must be man it must be man, and not a specialised set of experts among his fellows", but the familiar concept of man is dislimning and his common cultural inheritance is shredding away For, though the songs and stories of one half of the world are being sung and told in the other half, the highways—"the super highways"—which carry them leap over the village footpaths and the small roads that join one small community with another They are the means by which we are reminded of famine or war in remote places, but "they are also the means by which the true human community, the man knowing man, the neighbour understanding neighbour, the schoolboy learning a poem, the women dancing, the individual curiosity, the individual beauty, are being blown dry and useless The means by which the passivity of the disengaged spectator presents to the man of art and science the bleak face of inhumanity"

Like the artist, the scientist is separated from his fellows—"by long years of study, specialised vocabularies, arts, techniques, and knowledge, from the common heritage even of a most civilised society, and anyone working at the frontier of such science is in that sense a very long way from home" He is far, too, from the practical crafts in which his techniques, like the artist's, have their origins

In our somersaulting world we are stunned by the new things showering round us, all potentially good, some potentially dangerous beyond all former imagining

> "What is new," OPPENHEIMER said, "is that in one generation our knowledge of the natural world engulfs, upsets, and complements all knowledge of the natural world before The techniques, among which and by which we live, multiply and ramify, so that the whole world is bound together by communication, blocked here and there by the immense synopses of political tyranny The global quality of the world is new our knowledge and sympathy with remote and diverse peoples, our involvement with them in practical terms, and our commitment to them in terms of brotherhood What is new in the world is the massive character of its dissolution and corruption of authority, in belief, in ritual, and in temporal order Yet this is the world we have come to live in The very difficulties which it presents derive from growth in understanding, in skill, in power To assail the changes that have unmoored us from the past is futile and in a deep sense I think it is wicked We need to recognise the change and learn what resources we have"

What resources have we? He had an answer, an old sound one

> "We shall have a rugged time of it to keep our open and keep them deep, to keep our sense of b and our ability to make it, and our occasional ab see it, in places remote and strange and unfamili shall have a rugged time of it, all of us, in keeping gardens in our villages, in keeping open the m intricate, casual paths, to keep these flourishin great open windy world, but this is as I see t *condition of man, and in this condition* we ca because we can love one another"

This is, and always has been, practical adv hard to follow, and it does not come newly eve OPPENHEIMER, for he gave it last year, in hi Reith lecture,[1] perhaps with a less heavy heart.

> "As for ourselves in these times of change," h *then, "of ever increasing knowledge, of collective* p and individual impotence, of heroism and of drud- progress and of tragedy, we too are brothers"

He spoke too of the noble and spacious [illegible] science

> "We go in and out, even the most assiduous o not bound to this vast structure One thing w throughout the house there are no locks, there a shut doors, wherever we go there are the signs usually the words of welcome It is an open house, to all comers"

Is it still open? And how should it be kept He himself paid tribute to the universities, as munities in which artists, musicians, poets, scientists gather in fruitful companionship and e in the great task of teaching Here, if anywhere, doors in the house of science are unlocked [illegible] not unlocked everywhere, however, and it is wel we should keep this in mind, for there is a poi which the passivity of the disengaged spectator ca be distinguished from the passivity of the dazed by advancing headlights BERTRAND Ru in an unforgettable broadcast, has shown ou plainly—not as members of this or that c supporters of this or that form of government, as humankind

One question in particular needs a quick careful answer if science discovers secrets potentially dangerous that they cannot safely confided to humanity at large, to whom can they be confided? To politicians? To select comm selected on other grounds, probably, than their occupation with the good, the true, and the beauti Today we cannot act upon, and can barely d "man's right to knowledge and the free use there a concept perhaps worth dying for The doctrine—"man's right to secrets and the excl use thereof'—has triumphed in our heroic d and is fast creating a world fit for heroes, but heroes, to live in Does the nobler concept greater risks?

## Coloured Food

AT present, with a few specified exceptions any c ing matter may be added to food. The Food Stan Committee has now recommended[3] that the Public H (Preservatives, &c, in Food) Regulations, 1925–53, be amended so as to permit the use in foods of spe colours only Representations on the committee's re mendations may be submitted up till March 31 t joint secretary of the Preservatives Subcomm Ministry of Food Great Westminster House, Hor Road London, S W 1

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[1] *Listener* 1953 50, 1075

[2] *Ibid* 1954, 52 1135

[3] Food Standards Committee Report on Colouring Matters Stationery Office Pp 27 1s

# Annotations

## OUTLOOK FOR THE AMPUTEE

1950 the Ministry of Pensions set up a medical mittee with Sir Ernest Rock Carling as chairman to ider whether amputation of a limb, and subsequent ing of a prosthesis, can initiate or aggravate cardio ular disorder and whether such amputation reduces expectation of life These questions proved unex edly hard to answer An interim report published 951 was somewhat inconclusive and the majority rt[1] in 1953 brought in a new factor by suggesting men who have suffered major sepsis—with or with amputation—have a higher late incidence of cardio ular disease and an earlier average age of death he hope of putting its findings on a firmer foundation committee then arranged with the Ministry for the ical examination of some 5500 pensioners, of whom ) were to be amputees and 1000 were to be controls ortunately so many of this sample failed to attend no firm conclusions could be drawn

evertheless having reviewed the whole of the lence at its disposal the committee has now been able each some ultimate conclusions ' which seem fairly r On the question of expectation of life it says t starting for example with 100 amputees alive in 0 25 had died by 1950 compared with 23 of the eral population of comparable age and sex Of 100 unded pensioners alive in 1930 26 had died by 1950 npared with 24 of the corresponding general popu ion Both for the amputees and for the wounded sioners, the mean annual mortality rate was just r 1 per 1000 in excess of that of other people On the committee comments

> With so small a difference of total mortality the actual ribution among the certified causes of death assumes very e importance Some members of the committee think within the limitations of the statistical material available e is evidence of some slight excess of cardiovascular disease ompared with the normal population with a consequential iency of deaths from other causes. The committee as a le however are still of the opinion indicated in the rim Report that cardiovascular diseases have not been erienced more frequently to an extent of any significance ngst the causes of death in limb amputees as compared those with serious leg wounds without amputation
>
> Some amputees, especially those with a high thigh outation, necessitating a tilting table with excessive ity or with severe stump pain find the wearing of a thesis an increasing burden as age advances. These may rve individual reconsideration though other classes of sioner will also find their disabilities more burdensome the passage of time Neither as regards their mortality their morbidity do amputees form a class apart They e neither a higher mortality rate nor a higher cardio ular rate than other classes of seriously wounded

ving reconsidered the evidence on sepsis as a factor committee feels that the importance of this was over phasised in its last report It concludes with the owing answers to the questions put to it

> Limb amputations, and the subsequent wearing of a thesis do not in time produce effects on the body as a k which may initiate or aggravate cardiovascular rders to any significant extent There is no material rence between the mortality rates of amputees by reason amputation and that of the corresponding rates for sioners who have suffered wounds not leading to ampu ion Such excess as there is in both classes over that in the eral population is quite small. [2]

## APICAL LOCALISATION OF PULMONARY TUBERCULOSIS

As we recently noted[1] experimental evidence supports the hypothesis that the apical localisation of pulmonary tuberculosis is the outcome of relative anæmia due to the erect posture Dock[2] noted that the pulmonary arterial pressure was too low in comparison with the force of gravity to maintain flow in the upper third of the lungs of adults who were sitting or standing Thus few antibodies and macrophages were brought to the apex toxins were no longer diluted and removed and the resulting changes in gas tension by which $O_2$ tension is raised and $CO_2$ tension reduced were believed to favour growth of the tubercle bacilli in this region Dock[3] has now reviewed more recent work, which confirms the earlier findings with regard to the inadequate pulmonary arterial pressure in the erect posture, the changes in gas tension in the apical and lateral parts of the lungs with changes in posture and some of the effects of growing tubercle bacilli in altered concentrations of $O_2$ and $CO_2$ as found in systemic and pulmonic arterial bloods He also cites the observations of Scott et al[4] These workers anastomosed in monkeys a pulmonary or a lobar artery to a systemic artery or ligated a pulmonary artery or one of its branches (thereby also making the blood-supply systemic via the bronchial arteries) and showed that the lung or part of lung receiving systemic blood developed tuberculous processes more severely than the rest of the lung receiving pulmonic blood whether the tubercle bacilli were injected preoperatively (to give equal seeding all over) or postoperatively (thus giving heavier or earlier seeding to the pulmonic supply) whether inoculated with larger or smaller doses of bacilli or whether inoculated intravenously or subcutaneously in other words the higher $O_2$ tension in the systemic arterial blood was the chief factor in causing larger lesions, and changes in lymph flow were unimportant Dock states: Scott's experiments force one to accept the conclusion that only levels of gas tension are involved in protecting the base or in favouring tuberculosis at the apex This statement seems to take Scott's experiments rather out of their context Scott and his co-workers were giving the monkeys a primary infection with tuberculosis Dock is applying their results to explain the site of reinfection ' tuberculosis (autogenous or exogenous)—surely a very different and much more complicated problem

The present view[5] is that resistance of the body to invasion by tubercle bacilli resides in the mononuclear cells that accumulate around the bacilli assisted by unknown humoral factors Florey also points out[6] the difference between the reaction in an animal not previously infected and one previously infected or vaccinated and the earliest changes in animals are essentially the same as those in man In a previously uninfected animal during the first few days after inhalation of a few bacilli the organisms are taken up by mononuclear cells in the alveolar walls and multiply rapidly intracellularly without any surrounding cell reaction after eight days the cell reaction begins and this proceeds to necrosis During these first six to eight days the bacilli are known to spread along the lymphatics In a previously infected animal on the other hand a very active cell reaction starts in the first few days and the bacilli apparently remain unchanged in the mononuclear cells they are fixed to the site and do not spread along the lymphatics early In the human lung primary infection

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[1] Lancet 1953 i 633

[2] These conclusions are contained in a letter to the Chief Medical Officer of the Ministry of Pensions and National Insurance signed by the whole committee—namely Sir Ernest Rock Carling Dr A Greig Anderson Prof G R Cameron F R S Dr T I Cotton Prof J L D'Silva Dr A Hope Gosse Prof K J Franklin Dr W Ernest Lloyd Dr W P D Logan, and Dr [illegible] (secretary)

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[1] Lancet 1954 ii 1039

[2] Dock W Amer Rev Tuberc 1946 54 [illegible]

[3] Dock W Arch intern Med 1954 94 700

[4] Scott H W jun Hanlon C R Olson B J J thorac Surg 1950 20 761 Hanlon C R Scott H W jun Olson B J Surgery 1950 28 [illegible] Olson B J Scott H W jun Hanlon C R Mattern C F T Amer Rev Tuberc 1954 69 48

[5] Florey H W Lectures in General Pathology London 1954 p 601

[6] Ibid p 631

may occur at any site, if the infecting dose overcomes the natural resistance In people with acquired resistance, the factors responsible for this resistance cannot, owing to the erect posture, be brought so easily and in sufficient quantity to the upper thirds of the lungs (especially on the right side, because of the obtuse angle and longer branches of the right pulmonary artery), and because of the differences in gaseous tension bacilli grow most rapidly in the apical regions, and thus most lesions occur at the apex That the circulatory factor does not affect only the gaseous tension is also suggested by the collection of siliceous dust, and the resultant scars, at the apices,[7] where the particles in the macrophages stagnate though elsewhere they are removed by the bronchi and lymphatic channels This difference cannot be due to differences in gaseous tension

It seems unreasonable at present to regard one factor as solely responsible for the localisation of tuberculous lesions in the upper third of the lungs While Scott's experiments show the undoubted importance of differences in gas tensions in influencing the growth of tubercle bacilli, the factors involved in the host's resistance cannot be ignored Scott's experiments give no support to Smith's "stream flow" hypothesis[1 8]

## SUSCEPTIBILITY OF MENINGOCOCCI

THE change in the susceptibility of many strains of pathogenic staphylococci to penicillin (and in some cases to the antibiotics administered by mouth), and the emergence in the late war of sulphonamide-resistant hæmolytic streptococci and gonococci, point to the need for periodic re evaluation of the chemotherapy of infections Surprisingly, in meningococcal meningitis sulphadiazine has remained the drug of choice for upwards of fifteen years During the war time epidemics in the U S A the sensitivity of meningococci to sulphadiazine decreased very little,[9] and this decrease has never been shown to have materially affected the clinical response to the drug

Love and Finland[10] have tested the *in-vitro* sensitivity of 50 recently isolated strains of meningococci to eleven antibiotics and to sulphadiazine Weight for weight, penicillin was by far the most active agent and erythromycin ranked next, while polymyxin B and bacitracin were the least active Sulphadiazine, chloramphenicol, aureomycin, oxytetracycline, tetracycline, streptomycin, neomycin, and carbomycin had intermediate activity The strains varied within a narrow range in their sensitivity to each of the antibiotics, but their susceptibility to sulphadiazine varied over a wide range Of the 50 strains, 6 were moderately resistant to sulphadiazine according to the in vitro test used, but the remainder were completely inhibited by 50 µg per ml (5 mg per 100 ml) or less—which is well below the highest level of sulphonamide that can readily be maintained in the blood and cerebrospinal fluid of patients Even the 6 rather more refractory strains might have been inhibited by the dosage of sulphonamide used in Great Britain for severe infections[11] Comparison with the sensitivities of strains isolated and tested in or before 1945 gave no evidence of increasing resistance of meningococci to penicillin

It would seem from these results that sulphadiazine should still be the drug of choice in meningococcal meningitis, but that in the exceptional case where the clinical response seems to be delayed sulphadiazine might usefully be supplemented by chloramphenicol orally (since it penetrates well into the cerebrospinal fluid) or by penicillin intramuscularly and intrathecally

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[7] Dawson J Susman W *J Path Bact* 1937 45 597 Dawson J *Ibid* 1939 49 483

[8] Smith, D T Abernethy R S Smith G B jun. Bondurant S *Amer Rev Tuberc* 1954 70 547

[9] Schoenbach E B Phair J J *Amer J Hyg* 1948 47 177

Love B D jun Finland M *Amer J med Sci* 1954 228 534

anks H S *Lancet* 1941 i 104 M R C War Memorandum 10 H M Stationery Office 1943

## ELECTROLYTE DEPLETION IN PYLORIC STE

JUST as the hope of a universal *therapia magna* *sans*, aroused by the discovery of antibiotics, has dimmed by the emergence of bacterial resistance and sensitivity reactions, so the quest for "a few r rules" in treating electrolyte disorders seems d to failure because of the complexity of the di ances Commonly further disturbance is cre treatment directed at a single biochemical abnor The use of ammonium chloride to reduce a raised reserve[1] may be a case in point, for such treatment aggravate any concurrent depletion of base, and intoxication has in fact been observed in infant pyloric stenosis treated in this way[2] There may fallacies in arguing from the composition of the flu from the body to the likely electrolyte disorder, homœostatic mechanisms for one ion may be efficient than for another, so that the final res not be a simple subtraction of the fluid lost fr "normal" body fluid, but will be modified by in renal excretion of ions, and possibly by trans ions between cells and extracellular fluid

Black and Jepson,[3] in balance studies on p stenosis in adults, have defined the varied patter electrolyte depletion that may be found in patients, and they suggest that the raised alkali commonly found in patients with this condition be simply explained in terms of alkalosis conse loss of chloride in the vomited material During rec five patients with pyloric stenosis retained amount sodium, chloride, and potassium considerably than the amounts retained by patients who had un gone partial gastrectomy for peptic ulcer uncompl by stenosis The retention of base (sodium + pota was greater than that of chloride, suggesting that original depletion had been of base even more tha chloride The patients varied considerably in proportion of sodium to potassium in the retained some having been dehydrated and others retaining potassium than sodium In seeking to account disappearance of "alkalosis" observed on a régime actually provided more base than chloride, Black Jepson postulate that the alkalosis demonstrat extracellular fluid was matched by an even gr intracellular-fluid acidosis Evidence of this fea association with potassium depletion has been experimentally both in animals[4] and in man[5] F studies by Darrow's group[6] demonstrate that rats a high intake of bicarbonate will have an increased bicarbonate level only when their potassium inta severely restricted, and that the "alkalosis" induced can be corrected by potassium bicarbonate

These observations tend to emphasise deplet potassium rather than of chloride as the cause of e cellular alkalosis in patients with pyloric ste Potassium depletion has also been demonstrated in p stenosis by the finding of low serum levels,[7] by biopsy,[8] and by an observed increase in exchan potassium during recovery[9] Black and Jepson that administration of saline, which accentuates sium loss, should be reserved for patients wh clinically dehydrated Potassium salts should be by mouth, and there is some evidence that these absorbed even before the obstruction has been r by operation These workers condemn amm ide in view of the absence of any chloride deficit not ered ' by an equal or greater deficit of base In ion to the risk of water intoxication ammonium ide given in these circumstances might be expected nd to further loss of base from the body and to ivate the intracellular acidosis

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[1] Bodansky, O *Amer J med Sci* 1949, 218, 667

[2] Doxiadis S A Goldfinch, M. K. Holt, K S *Lancet*, ii 801

[3] Black D A K., Jepson R P *Quart J Med* 1954, 23,

[4] Cooke R E Segar W E Cheek D B, Coville F D C *J clin Invest* 1952, 31, 708

[5] Black, D A K Milne, M D *Clin Sci* 1952 11 397

[6] Cooke R E Segar, W E Reed, C, Etzwiler, D D Bruslow, S Darrow, D C *Amer J Med* 1954, 17,

[7] Lans H S Stein, I F Meyer, K A *Ann Surg* 195

[8] Mudge, G H, Vislocky, K *J clin Invest* 1949, 28,

[9] Moore F D, Edelman I S, Olney J M, James, A. H., L Wilson G M *Metabolism*, 1954 3 334

## VISCERAL EPILEPSY

CENT work on the electrical activity of the brain strengthened the clinical impression of over fifty ' standing that paroxysmal visceral disturbance sometimes be epileptic The syndrome is of interest everal reasons. First it is a problem in differential osis and if it is not recognised needless alarm and dominal operations may ensue Secondly the clinical ure is contributing to our knowledge of visceral esentation in the cortex the association of visceral psy with a local cerebral lesion or a focus of abnormal rtical discharge has shown that the medial aspect he temporal lobe is involved in visceral activity and ation Finally such cases display the linkage between psy and migraine for the paroxysmal visceral urbance of cyclical vomiting which is widely gnised as a prelude to migraine in adult life, is occasionally associated also with later epileptic cks, with or without migraine. Dr Wallis elsewhere his issue describes some cases of the condition His riptive term ' masked epilepsy ' is perhaps unfor ite since it harks back to a time when both the ical and the electro-encephalographic pictures of eral epilepsy were less well defined Nevertheless cases illustrate well the clinical setting and the gnostic pitfalls Usually the disorder first shows itself childhood and anticonvulsant drugs are valuable in diagnosis and in treatment.

## DIAGNOSIS OF PERICARDIAL EFFUSION

sterman and Thomas [1] have emphasised the value rapidly enlarging heart shadow on successive radio hs in the diagnosis of pericardial effusion but this is present only before all the fluid has formed, and the diagnosis may be more difficult Williams and tter [2] have reviewed a series of 17 cases all with iac tamponade and found that in 11 of these diagnosis was missed by at least one physician at the examination Symptoms were of little help for the monest—dyspnœa—suggested heart-failure or pul ary disease and cough was not a constant feature was present in half the cases, and only when this substernal and worse on respiration did it seem y to suggest the underlying condition Misconcep about the signs in cardiac tamponade were respon for the diagnosis being missed or rejected For mple often the apex beat was regarded as too easily or the heart sounds were thought to be too audible, any significant amount of fluid to be present while minent ventricular pulsations on fluoroscopy and of variation of the heart shadow with position ngly influenced other examiners A large effusion produce all the well known signs, but it does not riably do so and the classical quiet heart may be oncertingly loud and obvious. These misconceptions usually based on faulty textbook statements or nical lore handed on by teachers without verifi on but occasionally the physician was led astray his own common sense but incorrect deductions signs were often missed a rising venous pressure pul us paradoxus Increasing venous pressure missed usually because the physician expected ly distended neck veins in the upright position; iams and Soutter never found these but they did evidence of venous pulsation at the root of the neck ery patient but one They regard this as an important sign of raised venous pressure The paradoxical pulse although traditionally associated with tamponade, can occur in healthy people and be absent in those with an effusion It is best detected by careful measurement of the systolic blood pressure; a drop of 10 mm Hg or more during inspiration suggests its presence but this sign must be distinguished from the pulse alternation found sometimes in left ventricular failure

Although pericardial effusion causing tamponade is common early diagnosis is important, because treatment may be life saving and the diagnosis becomes increasingly difficult as the condition worsens with falling cardiac output and collapse Hæmopericardium should be borne in mind as a cause of tamponade; it has been described [3] as a complication of anticoagulant therapy for myocardial infarction and so may become commoner Here early diagnosis is especially important

## ENDOGENOUS VITAMIN $B_1$ DEFICIENCY

It is generally — and justifiably — accepted that Wernicke's encephalopathy is the result of aneurine (thiamine) deficiency In the great majority of cases [4] there is clinical evidence of lack of vitamin $B_1$ Experimental deficiency in the rat [5] and pigeon [6] and thiaminase induced deficiency in farm foxes [7] produce typical cerebral lesions In Japanese prisoner of war camps [8, 9] where the diet was deficient in aneurine the condition appeared like an epidemic Artificial aneurine-free diets produce appropriate symptoms in volunteers [10] and prevent recovery of alcoholics otherwise adequately treated [11] The lesions of the disease have been well described [12] and are highly distinctive Oddly enough the only aspect that is not fully agreed on is the clinical picture But so many of the cases seen under ordinary circumstances are complicated by other conditions producing cerebral symptoms of their own that this is not surprising The picture of alcoholic aneurine deficiency is particularly confusing, and the status of Korsakow's syndrome in particular needs clarification The simultaneous presence of other vitamin deficiencies also commonly complicates the picture But the careful studies of Phillips et al [11] have established that the cases in prisoners of war described by de Wardener and Lennox [8] represent the clearest-cut examples of pure cerebral aneurine deficiency yet reported

Against this more or less clear background Feigin and Wolf [13] claim to have found the lesions of Wernicke's encephalopathy in children with no vitamin deficiency These children were aged 2–4 years and presented a fairly distinctive clinical picture of a chronic disease with inadequate growth mental defect, ataxia and eye signs All appeared to have had adequate diets and at least one had been treated with large doses of aneurine All died and necropsy showed extensive lesions indistinguishable from those of classical Wernicke's encephalopathy in type and distribution (it is surprising to find the mamillary bodies unaffected in all three but they are by no means always involved) It is easy to criticise this work The number of proved cases of cerebral aneurine deficiency that have been examined at necropsy is too few for the comparison of the histological changes to be wholly reliable No biochemical studies—not even pyruvic acid levels—are recorded

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sterman F M M., Thomas G T Brit Heart J 1953, 15, 113
illiams C Soutter L Arch intern Med 1954 94 571

3 Goldstein R, Wolf L J Amer med Ass 1951 146 616
4 Spillane J D Nutritional Disorders of the Nervous System. Edinburgh 1947
5 Prickett C O Amer J Physiol 1934, 107 459
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7 Green R G, Carlson W E, Evans C A J Nutrit 1941 21 243 Sealock, R R Goodland, R L J Amer chem Soc 1944, 66 507
8 de Wardener H E Lennox B. Lancet 1947 i 11
9 Cruickshank E K Quart J Med 1950 19, 327
10 Williams R D Wilder R M Smith, B F Arch intern Med. 1940 66 785
11 Phillips G B Victor M, Adams, R D Davidson C S J clin. Invest 1952 31 859
12 Campbell A C P, Biggart J H J Path Bact 1939 48 245
13 Feigin, I Wolf A J Pediat 1954 45 243

But the cases are carefully presented and soberly discussed, and the authors' views deserve consideration They think it most probable that in these cases there was a congenital defect in the metabolic utilisation of aneurine—possibly a failure of phosphorylation to co carboxylase This view is slightly supported by the fact that two of their cases were sibs and the offspring of a consanguineous marriage

"Dysvitaminoses," among which this syndrome would be included, are in bad odour for instance, Flesch[14] has effectively disposed of so called local vitamin A deficiency in the skin But this should not lead us to prejudge this latest candidate

## DISLOCATION OF THE EYEBALL

EXTREME proptosis occurs when the equator of the eyeball passes in front of the plane of action of the sphincter-like orbicularis oculi muscle and the eyelids close behind the globe There are several causal factors One is trauma, and others are laxity of the eyelids and shallowness of the orbits In obesity with protruding eyes the trauma may be quite trivial, as in a case, recently reported, where separation of the eyelids to instil drops caused the dislocation[15] Negroes tend to have shallow orbits and so are prone to this mishap, and Lyle and McGavic[16] have recorded the case of a Negro with additional oblique muscles which, acting as protractors, allowed voluntary dislocation of the eyes Similarly, babies have shallow orbits and the eye may be luxated by injury at birth, or in a fit of crying, when the cause may be congestion of the orbital veins, especially if the baby has been held head downwards to terminate a choking fit

Dislocation of the eyeball usually causes blepharospasm, and the patient complains of nausea and a dull aching pain in the eye Replacement is effected by gentle and constant traction on the eyelashes with firm counter-pressure on the globe , it may be necessary to use a surface anæsthetic and to inject the facial nerve Rarely, lateral canthotomy may be needed Where the optic nerve and the extra ocular muscles have not been injured the patient is usually none the worse for his experience

## PELVIC CONGESTION

FOR some years H C Taylor, of Columbia University, has been applying to gynæcology the concepts of psychosomatic medicine He now describes[17] 100 cases which fall into the "more or less well defined clinical entity" which he calls pelvic congestion The entity is well defined mainly by reason of the multiplicity of the symptoms 20 complaints are listed, of which 11 are chief complaints The table begins with low abdominal pain, low-back pain, and secondary dysmenorrhœa , and the only constant physical sign is tenderness on pelvic examination But, while most gynæcologists will readily accept the existence of the group of patients whom Taylor describes, and may term them "functional," many may find difficulty in recognising the findings which he says are typical at laparotomy "the uterus is softened, slightly enlarged and purplish or mottled in appearance The cul de sac contains an increased amount of amber coloured fluid and there is recognisable œdema of the subserosal connective tissue and sometimes of the ovary" Surely many would regard such findings as normal Of his 100 cases, only 17 had a laparotomy during the investigation (though 47 had had a laparotomy elsewhere—as might be expected in such a group) Therefore in less than half his cases was endometriosis excluded Throughout Taylor's writings there is almost no reference to this condition, which would be strongly suspected by many clinicians o symptoms and signs he describes In his latest p the word endometriosis does not appear at all , an omission is especially strange since Meigs,[18] Scott Te Linde,[19] and many others have emphasised endometriosis is very common and seemingly o increase

Taylor outlines a tentative programme of th which includes "reassurance," the treatment of version and cervical erosions when present, advoc childbirth (which temporarily alleviates symptom finally surgery in which a choice has to be made resection of cystic ovaries and hysterectomy operation is undertaken a psychiatric consult arranged Theobald[20] has claimed better resul "cauterisation of the uterus plus" (following t of Young[21] who reported benefit from cauteris the cervix) He has extended the scope of the destruction by introducing a silver nitrate st the cavity of the uterus At the same time l dienœstrol 15 mg daily for six weeks and p containing "a pure active culture of the Met Bulgarian Bacillus"

If pelvic congestion and pelvic endometric clinically so very similar, it seems reasonable whether congestion, if long continued, may susceptible persons to endometriosis—the modern of women in the childbearing years

## NEW YEAR HONOURS

IN the past two or three years relatively few honours have been bestowed on members of ou fession in this country, and it is pleasant to see s notable medical names in the New Year list P Adrian's beautiful mind and public service have won him all the most coveted scientific distincti it is entirely proper that a peerage should nov him a member of a body whose primary function ception and where his experience will be value John Stopford, who becomes K B E , is likew experimental neurologist who has brought his into administration, and his contribution to the d ment of medical schools and hospitals has been less important than his work as vice chancellor chester University for the past twenty years new knights two hold chairs at Oxford P Le Gros Clark, though known most widely as an a on the primates, is an anatomist who has mai his stimulating contact with medicine, both by logical researches and through his lively school. I Macintosh's appointment in 1937 to the first chair of anæsthetics drew attention to the new imp of this specialty , and through his pupils, his w and his work in the Royal Air Force during the has had no small share in the remarkable devel of techniques in which British anæsthetists have lead At Aberdeen and since 1938 at Edinburgh Pr Davidson has combined special knowledge of blo orders with a broad outlook on medicine he is ph to the Queen in Scotland, and his knighthood co fitly with his presidency of the Royal Coll Physicians of Edinburgh We are likewise happ among the new knights the name of Mr A A. Ge of Liverpool, whose sterling work for the Royal of Obstetricians and Gynæcologists, both as pr and previously, has well deserved recognition A medical president whose knighthood we are glad is Dr Collins, president of the British Medical Asso in Australia

To all these, and to our other colleagues nan p 95, we offer warm congratulations

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[14] Flesch, P *J invest Derm.* 1952 19 353
[15] Offenbach B *New Engl J Med* 1954 251 338
[16] Lyle D J McGavic J S *Amer J Ophthal* 1936 19 316
[17] Taylor H C *Amer J Obstet Gynec* 1954 67 1177
[18] Meigs, J V *Ann Surg* 1941, 114 866
[19] Scott R B Te Linde R W *Ibid* 1950 131, 697
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[21] Young J *Brit med J* 1938 i 105

# Public Health

## N ALTERNATIVE TO HEALTH CENTRES

C O S Blyth Brooke
M.D Lond D P.H., Barrister at law
MEDICAL OFFICER OF HEALTH FOR FINSBURY

For a time after the National Health Service Act me into operation health centres were held to be the ost hopeful means of fusing the public health and general edical services Today enthusiasm for health centres s waned In practice it has proved difficult to find itable sites or premises and even when they have been ilt and equipped the expense of staffing and maintain g them would probably be out of proportion to their lue A large proportion of the cost would have to be rne by rates or taxes as general practioners could rdly be expected to contribute more than the saving practice expenses

If we are unlikely to have many health centres in the ar future we must look for other means of linking the miciliary preventive and curative services A possible lution to part of the problem, which might be to the lvantage of the profession and public alike would be r the public health department to offer the G P some f the facilities he might expect from a health centre—r example clerical help The scheme would undoubt dly place a small additional burden on the State and/or he local authority but this would be minute compared ith the cost of a health centre

### HELP FROM THE HEALTH DEPARTMENT

In essence the proposal means using the administrative t-up of the medical officer of health as offices for the P.s of the district

Every 3–4 G P.s would be allocated one clerk to act as rsonal assistant To ensure continuity of service—ring lunch intervals, sickness and holidays—each erk would have a deputy who might well be the clerk another group of doctors. The clerk would take down nd type letters prepare certificates for signature (when is was practicable) telephone to hospitals nursing sociations, and other agencies to arrange for and on half of patients and to inquire about them The ctors, during their surgeries or at other times might nd it convenient to telephone the health department for essages or to ask that letters be prepared for them to gn later Occasionally the clerk might visit the doctor s rgery to file his records. When it was convenient atients could call at the health department instead of e surgery for certificates and other papers.

The clerk might also make appointments for the doctor nd try to contact him or a substitute in an emergency n this way the public by ringing the health department ould be able to get hold of a doctor quickly: and the octor need no longer have his front door and telephone ontinuously attended Such arrangement might even e extended to the evening and night by using the services f a janitor

A dressing-station might also be set up near if not tually in the health department This would be staffed y a trained nurse who would do minor dressings for atients under the instructions of the family doctor nd the doctor might also attend himself He would us be relieved of time-consuming procedures in his rgery without sending the patients to hospital The atients would save time (an appointment system would e easy to arrange) they would be saved from e impersonal atmosphere of a hospital outpatient partment, and dare I say they would have their essings or at any rate their bandages, more skilfully pplied

An essential part of the scheme would be to set aside room which could be used by G P.s as a common room r dictating and signing letters This would soon ecome a centre where the M O H and his staff would have pportunity for discussion with the G P.s, encouraged perhaps by a supply of tea and coffee Notices on matters of medical or public health importance such as the local incidence of infectious diseases could be displayed, and a few current medical journals and recent textbooks supplied

### QUID PRO QUO

It might reasonably be agreed that as help was being given to the G.P s they should bear a substantial part of the cost it seems unlikely, however that many of them would consider it worth while to pay more than a nominal sum On the other hand they might well be glad to offer some services in return Each might accept the duties *of an assistant M O H to his own patients* It would be difficult at first to define the duties that the practitioner would undertake but I am sure some such plan helpful to both sides could be evolved

The G P could for instance do rather more than he does at present to keep the M O H informed of sickness trends in his practice He might supply details which did not involve breach of confidence on patients with non notifiable diseases of epidemiological importance or the subject of special study He would advise the M.O H and the social workers on his patients even when they were not attending him He could be asked to visit them to discuss the welfare of infants, control of infectious disease care of the aged and many other subjects Only in emergencies would he be asked to visit people not on his list—for example an aged person in need who was not on any doctor's list

In all these duties he would naturally work under the M O H but the services provided for his correspondence and the transmission of messages would be confidential

Possibly experimental arrangements of this kind could be organised under the present Acts by a liberal interpretation of the expression health centre If not a short amending Act would readily establish the legal basis on which a scheme could be developed

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## London in 1953

The dangerous situation which threatens now that the public has largely forgotten about diphtheria is again illustrated by figures given in the report for 1953[1] by Dr J A Scott medical officer of health for the County of London Despite continued publicity and further efforts by L.C C clinic doctors and health visitors the number of primary immunisations again fell during 1953, and the annual total was less than two thirds of what it was in 1949 It is estimated from the London figures that by the end of 1953 the proportion of immunised children under five years had fallen to 51 5%—its lowest level since the immunisation scheme came into full operation The report puts most of the blame on the apathy of parents and goes on to say "If the continuation of the present freedom from diphtheria is to be ensured the number of immunised children under five and particularly under one must be substantially increased without delay"

Among the vital statistics for London the report records a decrease in the death rate from 12 0 per 1000 population in 1952 to 11·6 in 1953 The cancer death rate continued to increase and there were more deaths from violence than in the previous year home accidents forming a disturbingly large part of the total The infant mortality rate was 23 9 per 1000 live births compared with 23 1 in 1952 25·4 in 1951 and 25·8 in 1950 The decline in the birth rate which has been going on since 1948 continues but it is slowing down in 1953 the London rate was 15·2 per 1000 population as against 15 3 in 1952 15·6 in 1951 15·7 in 1950 16·7 in 1949 and 13 4 in 1938

In 1953 of every 100 children born in London 88 attended a maternity and child welfare centre at least once in their first year of life—the highest recorded figure First home visits of health visitors to children under one were equivalent to 90% of the total live births The number of domiciliary confinements which has been declining since 1948 fell from

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[1] London County Council Report of the County Medical Officer of Health and School Medical Officer 1953 [illegible]

11,026 in 1952 to 10,472 in 1953 The total of midwives qualified to give analgesia has steadily increased and since 1950 all midwives employed by the council have been qualified to do so In 1946 analgesia was given in 3% of domiciliary confinements, in 1953 the proportion was 77%

One of the L C C's tasks is to keep watch on the condition of the water in the Thames, and its chemical branch makes a weekly examination at 25 points between Teddington Weir and the sludge-dumping area in the estuary—a total distance of 86 miles The pollution load that the river can stand obviously depends a great deal on the rate of flow, and it is laid down by statute that abstraction for water-supply shall not reduce the flow over Teddington Weir to below 170 million gallons per day The summer of 1953 was by no means dry, and the average daily flow for the months of July to September was 225 million gallons Nevertheless, the condition of the river became extremely poor and was bad over a considerable stretch of its course for many weeks, particularly between London Bridge and Gravesend But the report adds that new works for the additional treatment of sewage should shortly reduce the pollution load counteract the progressive deterioration of recent yea

## Northern Ireland in 1953

The Registrar-General for Northern Ireland[1] rep that in 1953 the general death-rate, the infant mort rate, and the death-rate from tuberculosis were lower than in any previous year The death rate w 10 7 per 1000 population—0 1 below the rate for 1 and 0 9 below the average for the five years 194 The cancer death rate of 1 54 per 1000 was, howe 0 07 above the five-year average, the annual numb deaths from cancer of the lung has more than dou since 1943 The death-rate from tuberculosis (0 23 p 1000 population) compares with 0 30 in 1952, and a f year average of 0 50 The infant-mortality rate of per 1000 live births was exactly half the correspon rate in 1923 The birth-rate (20 9 per 1000 populat was the same as in 1952

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[1] Annual Report of the Registrar General for Northern Ir for 1953 H M Stationery Office 3s 6d

# Special Articles

## HAZARDS AND HEALTH

In his report for 1953[1] the Chief Inspector of Factories (Sir George Barnett) records that the number of accidents (181,637) in premises within the purview of the Factories Acts showed the first appreciable increase since the 1939–45 war over the previous year's total (177,510), fatal accidents, however, decreased from 796 in 1952 to 744 in 1953 Several factors contributed to the rise in the total number, among them the increased number of man hours worked and the increase in the range of processes undertaken by women workers

Particularly disquieting is the increase in accidents to young people commenting on the persistently high figures in this group, the Chief Inspector states that "Allowing young persons to be injured or killed is a form of extravagance in which British industry simply cannot afford to indulge", and he quotes examples of accidents occurring "in circumstances so deplorable that one questions whether certain employers are fit to be trusted with 'this precious raw material'" "Lack of proper instruction of young persons," the report adds, "is the greatest single cause of machine accidents", and though the blame cannot always be laid at the door of the management, better discipline and closer supervision would prevent those avoidable tragedies which result from skylarking and youthful high spirits

Referring to eye injuries, the report draws attention once more to the difficulty of getting workers to use protective devices, whether provided statutorily or otherwise Much depends upon the attitude of the management if they make it clear that they treat the matter with the utmost seriousness, then the workers also will understand the importance of taking all available precautions The law, moreover, lays down that employers are obliged "not merely to provide the protection, but to exert all due diligence to see that it is used" Some factories have adopted the excellent practice of stamping job cards with appropriate reminders where the work demands special eye protection, and other firms have successfully organised intensive propaganda campaigns, but much more rigorous legislation is needed if the number of eye accidents (7738 in 1953) is to be reduced appreciably

The provision in all factories of first aid facilities has been compulsory since 1924, and though in some the legal standards have been far exceeded, in too many others the equipment consists of "small tin boxes covered with rust and dirt, containing the grimy remnants of their once statutory contents" Similarly, the standard of proficiency of first-aid attendants varies widely A factories employing more than 50 workers are requir to have a trained attendant, but the type of trainin not defined, and no stipulation is made regarding th time that may have elapsed since the course was unde taken The factory inspectors report an increas difficulty in recruiting volunteers for first-aid duti even where financial inducement is offered thi disturbing, and it is to be hoped that some way soon be found of impressing upon managements importance of this aspect of their workers' healt

The report draws attention to the difficulty of persua ing both employers and workers that a high standard cleanliness can and should be maintained even wh the trade is essentially a "dirty" one Too often c and rubbish are allowed to accumulate in anticipati of the "*great annual clean*" The larger factories are general better maintained than the smaller establi ments, and some of the cleanest are those in which th "dirtiest" trades are carried on Associated w cleanliness is the question of ventilation, and it encouraging to note that, with the rising price of fu more and more firms are installing modern systems heating which use waste products for fuel Ho in a large number of factories the heating and systems remain obsolete The report recommends th architects should give the same attention to the venti tion of factories as they now give so successfully concert halls, schools, hospitals, and other pub buildings

The Chief Inspector observes that health is not matter merely of protection against injury or diseas "if the individual feels that he is a unit, a clock numb or a cog in a machine, not even the best provisions for physical health will compensate for his sense of los recognition as a human being" Fortunately, there signs that managements are growing steadily aware of the need for promoting the mental as as the physical well being of their employees

## SENIOR REGISTRARS

### STATEMENT BY MINISTER OF HEALTH AND JOINT CONSULTANTS COMMITTEE

The Minister of Health has been reviewing the tra plan for senior registrars instituted in 1951 in the light the numbers actually employed and the factors which w affect the number of vacancies likely to occur in t higher grades in the period in which persons who enter t senior registrar grade in the next few years will completing their training

After discussion with the Joint Consultants Committ as representing the medical profession, the Minister h come to the conclusion that generally the intake of se gistrars in the various specialties is for the time being fficient to meet future needs and that the present mber employed should be maintained pending the out ome of the discussions in which he and the Joint Com ittee are engaged on the general subject of the medical affing structure of the hospital and specialist services

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[1] Cmd 9330 H M Stationery Office Pp 257 6s 6d

Accordingly in a letter of Dec 13 the Minister has ked hospital boards to maintain their senior registrar mplement in total and in each specialty at the number which it then stood subject only to a few minor terations

When a senior registrar completes the tenure of his esent appointment whether this is in a post within the aining plan of 1951 or in a 'transitional' post the nploying board is left free to extend his appointment for additional year so that he may have more time to mpete for a higher post if they are satisfied that his *tentialities are such that he is likely, given more time* obtain one When a post becomes vacant boards are pected to appoint to it a new senior registrar in the me specialty As hitherto there is nothing to prevent existing senior registrar from obtaining another nior registrar post in the same or a different specialty d holding it for the usual term

Senior registrars whose tenure is extended under these ew arrangements will of course continue to be free to ompete for higher posts It is emphasised, however hat their retention as senior registrars will not give them ny special claim or constitute any guarantee that they vill be successful

The Joint Committee have expressed their agreement vith these arrangements

## NEW YEAR HONOURS

The list of honours published on Jan 1 contains the ames of the following members of the medical profession :

### Baron

dgar Douglas Adrian o.m., m.d. Camb f.r.c.p.
President of the Royal Society master of Trinity College Cambridge

### K B E

r John Stopford m.b.e. m.d. Manc. f.r.c.p. f.r.s.
Vice-chancellor University of Manchester

### Knights Bachelor

ilfrid Edward Le Gros Clark m.a. Oxfd d.sc. Lond f.r.c.s. f.r.s.
Dr Lee's professor of anatomy University of Oxford

rchibald John Collins d.s.o. m.c. m.b. Sydney f.r.a.c.p.
President of the British Medical Association in Australia

eybourne Stanley Patrick Davidson b.a. Camb m.d. Edin f.r.c.p.
President of the Royal College of Physicians of Edinburgh professor of medicine University of Edinburgh.

rthur Alexander Gemmell, m.c., t.d. m.a., m.d. Camb f.r.c.s.e.
President of the Royal College of Obstetricians and Gynæcologists ; gynæcological and obstetrical surgeon to the United Liverpool Hospitals.

obert Reynolds Macintosh d.m. Oxfd f.r.c.s.e., f.f.a. r.c.s.
*Nuffield professor of anæsthetics University of Oxford*

### C B (Military)

ajor General Charles William Greenway c.b.e. m.r.c.s. q.h.s.

rgeon Rear Admiral James Hamilton c.b.e., m.b. Glasg

### C B (Civil)

on Walter Symington Maclay o.b.e. m.d. Camb., f.r.c.p.
Senior medical commissioner Board of Control

### C.M G

ril Francis Fernando o.b.e. m.d. Lond m.r.c.p.
Physician General Hospital Colombo

aymond Lewthwaite o.b.e. d.m. Oxfd f.r.c.p.
Director of Colonial Medical Research.

### C V O

Joseph Graeme Humble m.r.c.s.

### C.B E (Military)

Surgeon Captain John Henry Bruell Crosbie, m.b. Dubl., r.n. retd.

Major-General Frederick Cavendish Hilton-Sergeant m.b. Lpool q.h.p.

### C B E (Civil)

Arthur Frederic Alford m.d. Brist
Senior medical officer Ministry of Education

William Edward Lodewyk Hamilton Crowther d.s.o., v.d. m.b. Melb f.r.a.c.p.
Hon consulting physician Royal Hospital, Hobart president Medical Council of Tasmania.

Maurice Walter Goldblatt m.d. ph.d. Lond
Director industrial hygiene research laboratories Imperial *Chemical Industries Ltd*

Joseph Harold Sheldon m.d. Lond f.r.c.p.
Director of medicine and senior physician, Royal Hospital, Wolverhampton

Denis John Williams, m.d. Lond. d.sc. Manc f.r.c.p.
Civilian consultant to the R.A.F in neurology and electro-encephalography physician in charge of neurology St George's Hospital

### O B E (Military)

Surgeon Commander Thomas Wilson Froggatt m.b. Sheff r.n.

Lieut Colonel John Irvine m.b. Glasg., r.a.m.c.

Lieut -Colonel Thomas McGregor McNit m.b. Glasg., m.r.c.o.g. r.a.m.c.

Wing Commander John Hope Pool, m.d. Durh r.a.a.f.r.o.

### O B E (Civil)

Basil William Armstrong m.c., m.b. Lond
Lately medical superintendent Royal Sea Bathing Hospital Margate

David Alexander Baird m.b. b.sc. Edin
Director of medical services Somaliland.

Arthur Beauchamp m.b. Birm
General practitioner Birmingham ; for services to the Ministry of Health

Eliot Cecil Curwen m.a., m.b. Camb
Hon physician Police Convalescent Seaside Home Hove.

Weliwattage Livtris Perera Dassanayake l.r.c.p.e.
Superintendent filariasis campaign Ceylon

William Marsden Ford Robertson m.d. Edin
Medical director Lebanon Hospital for Nervous and Mental Diseases, Beirut

Thassos Charidimou Gircotis m.d. Vienna
*For medical services in Cyprus.*

George Rajanayagam Handy m.b. Lond
Visiting physician, General Hospital Colombo

William Edward Hutchinson e.d. m.d. Dubl j.p.
a.d.m.s. (civil defence) Singapore

Edward Norman Jamieson f.r.c.s.e.
Surgeon Lewis Hospital Stornoway

James Hutchinson Kennedy d.m. Oxfd
Government medical officer at Ndanga Southern Rhodesia

Arthur Gentry Pitts f.r.c.s.
Medical practitioner Waimate New Zealand.

John Herbert Owen Roberts m.d. Lond j.p.
Medical superintendent North Wales Hospital for Nervous and Mental Disorders, Denbigh

Loris Rohan Sharples m.b. Edin.
For public services in British Guiana

Walter Ansley Young m.r.c.s. j.p.
For public services in the Federation of Malaya

### M B E (Military)

Major Thomas Charles Ayres t.d., r.a.m.c. t.a.

Captain Ivor Robert Bessant r.a.m.c. t.a.

Captain Alexander Joseph Zosimus Navaratne Ceylon Army Medical Corps

Squadron Leader Ernest Sidney Odbert m.b. Dubl., r.a.f.

Major Leslie Frank Richmond t.d., m.d. Durh., r.a.m.c., t.a.

### M B E (Civil)

Mona Kathleen Bailey (née Blackall), M B Sydney
Medical practitioner in the Australian Capital Territory
Frank Howard Budden, M B Lond
M O (ophthalmology), Northern Region, Nigeria
Maria Leonora Du Toit
For medical services in the Tiv division, Northern Region, Nigeria
Jane Evans
Medical missionary in Egypt
Lucien Arnold Gunesekera
Medical practitioner, Colombo
James Donald Holmes, M B Glasg
Admiralty surgeon and agent, Finchley and district, London
Thomas Affleck Morrison, M B Aberd
Chairman, Brighton Executive Council
Charles Vincent Mtawali
African assistant M O, Tanganyika
Ida Mirrielees Seymour, L R C P E
Lately medical officer, Department of Health for Scotland

## Medicine and the Law

### Capital Punishment

Mrs Styllou Christofi, a Cypriot, was charged with the murder of her daughter in-law She spoke practically no English and her trial was conducted with the aid of an interpreter She was found guilty and sentenced to death at the Central Criminal Court on Oct 28 An appeal to the Court of Criminal Appeal failed, and the Home Secretary decided not to recommend a reprieve She was executed at Holloway Prison on Dec 15

The hanging of a woman is comparatively rare this is only the third case since the war The case is unusually important for two reasons

First, there is some doubt as to the woman's mental condition, particularly at the time of the murder Dr Thomas Christie, principal medical officer at Holloway Prison, in a report dated Oct 5, said that after observation of the prisoner since July 30, he had formed the opinion that she was insane, but was medically fit to plead and stand trial He wrote[1]

> "The clinical picture is that of a non systematised, delusional mental disorder This is a disease of the mind In my opinion, the fear that her grandchildren would not be brought up properly induced a defect of reason due to the above disease of the mind whereby, however much she may have been capable of appreciating the nature and quality of the acts she was doing, at the time of the acts the defect of reason was such that she was incapable of knowing that what she was doing was wrong "

If Dr Christie was right in that opinion, then Mrs Christofi was insane within the meaning of the McNaughten rules A copy of his report was furnished to the defence, but on the prisoner's own instructions the defence did not raise the issue of insanity As she was deemed fit to plead, counsel had no option but to accept her instructions

After the prisoner's appeal had been dismissed, the case came before the Home Secretary If it appears to the Home Secretary that there is reason to believe that a prisoner under sentence of death is insane, he must by the Criminal Lunatics Act, 1884, appoint two or more legally qualified medical practitioners to examine the prisoner and to inquire as to his insanity In view of Dr Christie's report, the Home Secretary appointed three doctors to conduct an inquiry They reported, according to the Home Secretary's explanation in the House of Commons,[2] that Mrs Christofi was not in their view insane, and they added that in their view she did not suffer from any minor mental abnormality which would justify them in making any recommendation on me grounds relevant to the question of a reprieve T Home Secretary also disclosed that Mrs Christofi w not agree to electro encephalographic examination

Secondly, this case raises again the question of Home Secretary's responsibility and his relations Parliament At the time of the Bentley case,[3] the Spe ruled that a particular case could not be raised in House prior to reprieve or execution, but that a reprieve or execution the Home Secretary was an able to the House This ruling has obvious disadva in that execution settles a case beyond recall, but t are clearly reasons for it In the Bentley case, how the then Home Secretary, Sir David Maxwell Fyfe, receive deputations of M P s

In the present case the new Home Secretary refused receive such deputations, although he agreed "a exceptional step " to see Mr D Weitzman, Q C, M P, was counsel for the defence at the trial When questi about this in the House after the execution, he sa "I am sure that, while it is of course open to Membe Parliament to submit representations to the Secretar State, the House will agree that a Home Secretary sh not be expected to receive oral representations, even fr hon Members, and to discuss the case with them, wh he is engaged in the discharge of this onerous and an duty " After the execution, the Home Secretar asked to publish all the medical evidence and the ad given to him by the trial judge The Home Secret replied that he was not prepared to make these doc available, it would, he said, be contrary to established practice and open to considerable objectio

The Home Secretary's refusal to publish the docume makes it difficult to form a judgment on this case leaves certain questions unanswered For instance, i not clear whether the Home Office doctors expre dissented from Dr Christie's opinion that Mrs Chris was insane at the time of the murder, or whether they principally concerned with her mental condition at t time of their examination When insanity is plea at the trial, *the court is concerned solely* with t prisoner's mental state at the time of the murder, but t Home Secretary in considering a reprieve may a take into account the prisoner's subsequent mental sta

Publication of the report of the Home Office doct would have been valuable in another connection I Mrs Christofi pleaded insanity, that defence might have succeeded in view of Dr Christie's report It likely that Mrs Christofi threw away her best li defence That raises the question of how far a pris as to whose sanity there is some doubt, is the best pe to decide his or her defence It is difficult to see that right can be taken away from a person deemed to plead, and for that very reason the prerogati mercy assumes an especial importance

The legal and administrative difficulties involved these cases would disappear if there were no death pen

### Death after Ambulance Journey

The death of a 72 year old man after transfer a sitting case by ambulance from Glasgow Royal Infirm to Helensburgh Victoria Infirmary was the subjec a fatal accidents inquiry in Glasgow on Dec 23[4] jury returned a formal verdict that the man had as a result of a broken rib puncturing his lung d the journey The widow gave evidence that her hus had become very ill while sitting up throughout journey A doctor from the Royal Infirmary s that he had given instructions for the man to be tr ferred as a stretcher case A pathologist who had a necropsy said that if the patient had travelled l down the movement of the rib would have been redu

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[1] *Daily Express* Dec 15 1954
[2] See *Lancet* Jan 1 1955 p 53
[3] *Ibid* 1953 i 279
[4] *Glasgow Herald* Dec 24, 1954

## A Letter from the Hospital

t an inquest in Doncaster on Dec 20[1] the coroner urned a verdict of suicide while the balance of the ud was disturbed in the case of a 30-year-old woman o had been found gassed in the kitchen of her home coroner said that there was a history of mental ess since the birth of a baby in October The woman been admitted as a voluntary patient to Middlewood spital, Sheffield and, according to evidence at the uest, on the day of her suicide she had opened a er from the hospital addressed to her husband ing that her condition had not improved The oner wanted to know why the letter was sent to the nan's home instead of to her doctor and why it merely a typed document with blanks filled in and ed by the clerk." 'I do not think,' he declared here is any doubt it had the final effect of making lose her balance and I think there is no question atever she decided on the spur of the moment to take life in consequence

n official of Sheffield no 2 Hospital Management mittee, whose group includes Middlewood Hospital eported to have said that the medical superintendent considering whether it might be advisable to omit reference to the patient's condition from the form t to the relatives The letter mentioned at the inquest s a statutory form laid down by the Board of Control

## Habit forming Drug

The habit forming characteristics of pethidine were erred to in a recent case in which the wife of a doctor s granted a decree for the restitution of conjugal hts[2] The husband's cross petition for divorce on the und of cruelty was rejected

he parties were married in 1941 Between 1948 and late in the wife underwent a number of serious operations and health began to deteriorate After a major epileptic fit 052 she was admitted to The Retreat York and after it three months treatment was formally discharged The wing year she again entered The Retreat and while she there the husband wrote to her that in no circumstances ld she be admitted to his house again and refusing to let see their child—a letter which said Mr Justice Wallington, ated the husband's determination to bring the marriage n end

ealing with the husband's allegations of cruelty his Lord said that it was common ground that the acts alleged due to the fact that late in 1951 the wife became a drug ict after injections of a particular drug given to her after operations. It is a synthetic drug and it was not realised some time after it appeared on the market that it was a t forming drug The judge said that he was satisfied the wife had acted to some extent as the husband had ed She pressed him for injections disturbing his rest acting him when he was attending his patients during day making him less confident in his work and less fresh ind and body

ere came a time said the judge when the husband knew out pethidine The time came when he injected the drug a frequency which he knew must have a disastrous effect is wife I am not charging him with doing anything iously wrong He was in a great difficulty and he had oose between losing his sleep and the disturbance of the and giving his wife a drug which would make her quiet dealing with this case on the footing that he did not ything which he knew to be morally wrong He was kind to her because he did not like to see her suffer "

e husband his Lordship continued had never suggested he was prevented from carrying on his practice apart from wn two illnesses, although he might have been hindered describing some of the husband's evidence as exagger to the point of improbability the judge said: I cannot that the husband has proved any danger to his health or mental as the result of the wife's conduct His ges of cruelty therefore fail

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[1] *Star, Sheffield* Dec 20 1951

[2] *Yorkshire Post* Dec [illegible] 1951

# In England Now

*A Running Commentary by Peripatetic Correspondents*

GRANNIE's passion for locks and keys was a source of unending amusement in the Smith family On her bedroom door was a Yale lock two bolts, and a hook and-eye catch Her small bureau for her papers was reported to be a honeycomb of secret drawers. She kept her keys in a purse under her pillow and in the three years I visited her I never knew her to lose grasp of this purse Indeed I believe she slept with her arthritic fingers firmly locked around it It was not that she was ungenerous; her grandchildren adored her: but she had a fixture for locks and keys. Just as many ageing folk develop a fancy for acquiring things, hoping that an accumulation of life's trappings will give them a surer hold on life itself so Grannie put away, firmly closed and locked everything hoping perhaps, to conserve and extend her own contracting days

Once when her purse burst open and her keys fell in a shower over the bed I laughed and said 'Grannie, I can see every key except the Key to the Kingdom of Heaven! Gravely she pointed to her heart and said I keep *that* one locked in here

She had a great fear of hospitals and made me promise more than once that I would never send her there It was therefore with a troubled mind that I read the pathologist's report *S typhi* isolated. I told the family that I did not think we should be sentimental about her distrust of hospitals and that I meant to send her to the isolation unit as soon as possible They were, of course in agreement. So I went upstairs to her bedroom and sat on her bed and took her hand and said Grannie I am afraid I must break my word You have got a serious illness which you could pass on to the family I have arranged for your admission to hospital. She gave me a long steady look which I shall not forget.

Before the ambulance came she gave her daughter all the keys, commanded her to unlock every lock and open every drawer and box and cupboard in the room She gave precise instructions how to slide back the panels which revealed the secret departments in her bureau Most of the drawers were empty Some contained a small amount of paper money old letters tied with ribbon, her dead husband's tobacco-pouch now containing crushed lavender, a few trinkets.

By this time the ambulance had arrived and with great composure she lay on the stretcher As she was being taken out of the door her daughter rushed up to her and said I will bring up all your keys later Grannie I have the only one I need, she said

* * *

I had a Greek girl in outpatients yesterday and asked her if she was breathless She didn't understand so in despair I asked if she had dyspnoea. Ah yes she said I have dyspnoea and you speak Greek.

* * *

The DC 3 glided to a halt in front of the little airport buildings and I stepped out into the glare of the Colorado sun feeling very British and conspicuous in my dark lounge suit among the light summer attire and gaily coloured shirts around me There was something remarkably fresh and invigorating about the air and the expanse of open country around the airport after the noise exhaust laden atmosphere and urgency of Chicago My host from the hospital was waiting and after a quick lunch he suggested a short sight-seeing drive This proved to be a modest run of 180 miles over arid desert through the picturesque little town of Montrose so different from its Scottish namesake to the Black Canyon of the Gunnison The forbidding grandeur of this grim canyon the beauty of the lakes and coniferous forests at the top of the Grand Mesa and the red magnificence of the rock formations of the Colorado National Monument which we visited next day defy description

But my visit was a professional one; the local medical society dinner was planned for 7 P.M my lecture for 8.15 P.M and at 6.50 P.M we were at the hospital The secretary of the society met us looking a trifle sheepish I'm sorry he said but the cooks thought the dinner was tomorrow night The society put its heads together and decided we should go to the president's for liquid refreshment and to think things over We climbed into roughly fifteen cars and descended upon the president's wife, who responded manfully, as American wives do At 7 45 P M it was decided that we should dine at the local restaurant, which for so small a town was remarkably sumptuous Conversation flourished, except when I mentioned the National Health Service By 8 45 P M our numbers had risen to roughly fifty, we were on Christian name terms, and the society decided that perhaps I ought to be delivering my lecture We straggled back to the hospital, and were entering the lecture room when Joe realised that he had forgotten the projector Jake sprang into the breach and into his Jaguar, and was back within ten minutes carrying a small black box, which, on being opened, unexpectedly proved to contain an electric sewing-machine But in due course another box was produced, this time the right one, and Jake atoned by acting as projectionist At 9 15 P M, provided with a broomstick to use as pointer, I began my lecture Faced with a professional topic, the audience subsided into gloom, which was rapidly dispelled a few minutes later, when the screen fell over Whether my subject interested my audience, I cannot tell, but I certainly enjoyed the evening

* * *

All men wear trousers in public, and most accept the convention of having them done up In the old days the loss of a button mattered little and the defect could be quickly remedied at home at the end of the day But with the introduction of modern closing techniques the situation has become potentially dangerous

Lately, while visiting a famous foreign clinic I had occasion to leave the room between cases, whereupon the most vital of all zips literally came off in the hand All efforts to restore the situation were fruitless Return to the clinic was unthinkable, it was too long to wait, at any rate there, and the possibility of a message to the operating-theatre for a row of Michel's clips occurred to me too late Action was imperative, and for better or worse I decided on flight Simulating confidence, looking neither to right nor left and with head erect—to increase anterior tension—I reached the hospital exit without apparently attracting attention

As luck would have it at the first corner was a clothing store But inside was a woman choosing ties for her husband She was in no hurry and the assistant showed signs of waiting to leave her to make up her mind and attend to me I feigned interest in a box of socks farther down the counter When the opportunity for explanation finally came the assistant regretted that they had no facilities for repairs but suggested a tailor farther down the street This meant another public appearance but again I excited no undue attention The next hazard was the least expected The only attendant behind the counter was a woman Flight seemed ridiculous She was middle-aged, of kindly demeanour, and wore a wedding-ring I outlined the general position She explained that the tailor himself was ill but that there was another four blocks away This distant craftsman proved to be male, but a heartless scoundrel who took full advantage of my situation zips were irreparable, he declared, and he was too busy to insert a new one that day, he advised me to buy a new pair of trousers I pointed out that none of his trousers matched my coat He replied that non-matching trousers were the current fashion in America Finally he suggested a row of safety pins and scornfully declined payment Walking delicately, like Agag, I was now able to return to the clinic, but explanations caused more entertainment than sympathy

* * *

I like to go to Guidance Clinic
And be a charming little cynic
And paint the walls all scarlet red
And hit caretakers on the head,
For this reveals my true intents
And latent talents, and prevents
The insalubrious suppression
Of all my long pent-up aggression
I like to paint the Clinic red
And hit caretakers on the head,
But, mother figure, is it true
There's *nothing* that I mustn't do?

# Letters to the Editor

## SANATORIA

SIR,—The leading article in your issue of De suggests, on the basis of some American evidence, t the introduction of antibiotics has rendered ob a good deal of sanatorium treatment

No worker in the field of tuberculosis can doub value of the new antibiotics but they have been i duced against a background of better nutrition am the poorest classes, financial arrangements that p a patient to rest in a sanatorium without eco catastrophe, the raising of the standard of trea throughout the country to the level previously en only by a few areas, enormous improvements in much wider application of surgery, and a better u standing of pathology

To treat a lesion instead of a patient is always medicine in tuberculosis it is a disaster Yet, in as if some of the patients could not be safely treated drugs whilst they work, your leader suggests pro this fallacy In any case, we know the answer It been my lot to have referred to me a considerable nu of doctors suffering from this disease Owing to quaint but widely held belief that disease always a different course in the medically qualified, they in many cases been treated by antibiotics whilst tinuing their work Without exception, they deteriorated on this régime

A young man or woman may acquire tuberc because of an overwhelming infection by a close co whilst in a susceptible state or because of greatly l physical resistance, as in semi starvation condition example, in a prisoner of-war camp More comm however, the disease arises because resistance to e genous or exogenous infection has been lowered domestic or financial difficulties, by driving ambit excess of ability, or by failure to adjust to environ If an initial minimal lesion is controlled by drugs o out by a surgeon, but the resistance not raised and te not released, further lesions are likely to arise To a patient, a sanatorium régime, if sympathetically skilfully applied, will not only enable him to overcom current infection, but will induce a state of mind a philosophy that will afford a considerable meas protection for life Whilst the smell of pine needl a rarefied atmosphere do not affect the tubercle ba directly, I do firmly believe that a patient will r more permanently if he watches the serene bea forest and meadow from his bedroom window, th he passes several months of enforced idleness lo at a factory chimney

The abandonment of country sanatoria may necessity, but let us not try to make a virtue of it of them may be unfit for the middle aged it wo a wise investment to rebuild them The Norwegia emptying their sanatorium beds but only becau are eradicating the disease and not because the keeping their active cases at work

You question the wisdom of confining "non mi young people for months in surroundings wher suffer the possibly adverse effect of being surr by others with the same disease" If the adverse referred to consists of mental depression by co from despondent "chronics," then the sanatorium indeed be a badly managed one

Finally, may I stress as axiomatic that a p who is ill enough to need treatment with antib ill enough to be in bed

Liverpool LESLIE J TE

SIR,—Your editorial does not pay the credit due late chief, Sir John Robertson As medical off h for Birmingham he it was who had learnt and ht the value of George Bodington s work, and who tuted the campaign against tuberculosis including building of the sanatoria The emphasis he placed sanatoria was in mental and physical rest in pure vith good food and where the patient s home was of right standard he regarded it as the safest and place in which to treat infectious disease The ment of pulmonary tuberculosis was to include ing unpleasant but everything which brought rest fort, cheer brightness and fresh air to the patient his family and the family doctor was the best on to undertake it

s the tuberculosis service has developed I have ched the progressive departure from these ideals tuberculous patient has gradually been taken out he hands of the family doctor by the institution pecialised techniques—pneumothorax pneumoperi um phrenic nerve paralysis thoracoplasty—and t is still more important these measures have been oted as substitutes for rest (e.g if a patient could not found a bed in a sanatorium pneumothorax was iced to rest the lung) After hundreds of thousands of ents have been treated by this means we are now that they are of little use—lung resection and acoplasty are the correct treatments But not while patient has an active focus for operation at such a can spread the infection to normal lung lung ction must not be done until the lesions have healed patients now admitted to sanatoria are told that r when they have recovered they may have to have r lung removed As Dr Houghton and Dr Corrigan ted out the patient who enters a modern sana um can no longer contemplate a period of tranquillity freedom from personal anxiety Modern sana um treatment has caused people to look upon the ase with horror therefore let us get back to teaching of Sir John Robertson Give the patient the comfort and cheer and restore the family doctor to rightful place We can the more readily do this now we have efficient drugs

mingham 15 JAMES F BRAILSFORD

IR —Your leading article poses several questions of t importance The picture as you say has been oundly changed by the antibacterial drugs and it is ly for many of the old methods to be re-examined case of the tuberculous child must, however receive ial consideration

Whilst it may be reasonable as you suggest to treat am adults with small uncavitated lesions with rs while they work this method should not be sidered in the case of school-children except under the t careful safeguards These small uncavitated lesions dult type disease in adolescents demand the closest ntion They are likely to be recent and tend to gress and spread if not dealt with energetically

For should there be any questions arising in the case children about the irritations of institutional life the possibly adverse effect of being surrounded by rs with the same disease Whilst far too many ur boys and girls still become infected with tubercu only a small proportion of the cases that come to call for prolonged institutional treatment In this p should certainly be included the rare cases of lren with adult type disease These should be itted only to sanatorium schools fully equipped both leally and educationally

obably it is true to say that tuberculous children tered in small numbers and isolated groups through the country have been neglected in the past ainly this is the case today for from time to time ig people with tuberculosis are admitted to my torium who have received previous treatment in surroundings quite unsuited to their tender years and educational needs. Numerically the problem of how best to provide for these handicapped youngsters is small Probably half a dozen comprehensive centres would cover the needs of the whole country The names of two or three readily suggest themselves All that is required is a little interest and understanding of the problems involved at the appropriate administrative levels

High Wood Hospital for Children,
Brentwood Essex. F J BENTLEY

## HÆMOLYTIC TRANSFUSION REACTIONS

SIR —I do not understand why when blood transfusion is to be discussed, so many protagonists entangle them selves with arguments on blood grouping True blood grouping is an important factor in blood transfusion but it is only one factor among several such as the collection of donor blood, its storage distribution and adminis tration and I cannot admit its pre-eminence among these Blood transfusions are given to save lives and it is our duty to remember this and not to waste our energy on sterile recriminations No two patients have the same needs, no two hospitals the same patients One hospital may receive no emergency admissions and have but a limited number of elective operations in such a hospital blood grouping can be done by the most elaborate and time-consuming methods without harm to any and with benefit to all Another receives patients from a large sparsely inhabited tract of land the patients who survive the journey to hospital will readily tolerate two or three more hours delay so slow methods may again be used (though I think a flying squad using rapid methods might not be out of place) In a city a hospital may receive all the emergency work – traumatic as well as medical—from a population of 250 000 within a radius of 3 miles here patients more often survive the journey to hospital but may arrive in the receiving room grey pulseless with air hunger and barely conscious It is for these and those a little less ill that I am con cerned : and it is with such patients in mind that I decided eight years ago that I must provide a blood transfusion service which would tolerate only the minimum of delay

During these eight years although I used the more complicated methods freely I have depended chiefly on the simplest methods So far I have killed no one, though I have made a dozen blunders but I have found that every one of these dozen blunders was due to a failure of the human element—not to a failure of the simple method being used Every blunder was revealed by simple repetition of the test by someone working without anxiety or preoccupations—often by the person who made the original mistake I therefore offer no apologies for my crude methods, for crude ' they may be called though they revealed an anti-c and an anti r

Besides this ethical problem (for I claim that these rapid methods probably save half a dozen lives a year and add only infinitesimally to the danger of trans fusion) there are the various practical points which have been brought up in this correspondence Dr Taylor (Dec 18) and Dr Walther (Dec 25) believe that tube methods are so much more reliable than any others that they must be adopted I would refer them to one paper [1] which shows that in some conditions tile methods for ABO grouping may be more reliable than tube methods and I would remind them of the method of the inclined capillary tube for Rh testing [2 3] one of my colleagues has performed [4] a direct comparison with the tube method on 2500 samples without a discrepancy The data indicate that the reliability of a serolo may vary with the surroundings in which it is performed, that a method ideal for the unhurried reference laboratory may prove less satisfactory in the busy routine laboratory Dr Walther advocates the more general use of group O rhesus negative blood, but I fear that it would prove impossible to supply the quantities required, and since it can give rise to hæmolytic reactions it would prove little, if any, safer than the simplest methods of grouping and cross-matching

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[1] Allen, F H jun Diamond, L K Mad I n J Med 19 1 244 9
[2] Chown, B., Lewi M J cl n Path 1951
[3] Discombe G Meyer H Amer J clin. P
[4] Jacob G F Personal communication

Dr R M Heggie (Dec 18) is mistaken when he suggests that representations by any pathologist can produce an improvement in laboratories or increase of staff overnight, and that inadequacy of laboratory and staff is the fault of the pathologist Too often the pathologist's appeals for staff and space are suppressed in the medical advisory committee or refused by the management committee, and even if his pleas are granted, there must be a delay of years before buildings are erected or staff trained No pathologist can appeal to the regional hospital board over the heads of his colleagues, and if he appeals over the head of the hospital management committee, he is unlikely to obtain any satisfaction It is not fair to impute all the blame to the pathologist and to exculpate the administrator who fails to provide essential facilities

The actions of Dr J F Heggie and his committee seem to have been beyond reproach, not so those of the other bodies who circulated that memorandum There is real and widespread dissatisfaction over the dissemination of these memoranda, but this dissatisfaction could easily be overcome by the Ministry or the regional boards Every hospital management committee should be instructed to arrange for the regional transfusion director to consult with the pathologists responsible for blood-transfusion in that group, and to submit agreed and detailed recommendations on the space and staffing needed to provide an adequate service, and on the *deviations from optimal techniques which would be* needed to utilise best the existing facilities Differences of opinion would of course arise, and these could most easily be settled with the aid of members of a panel of specially experienced pathologists nominated by the Association of Clinical Pathologists

I suspect that some of the warnings given in memoranda are open to question Dr Taylor praises Dr Heggie's warning about infected blood, but I understand that Dr Heggie's experience of such accidents is limited to three cases when I encountered one of these in the High Court, the evidence suggested that the death was not caused by infected blood One should realise that the whole North London Transfusion Service has had one death from infected blood in five years, during which period more than 500,000 bottles were issued The evidence on which warnings are based should be published [5] and not restricted to some coterie of initiates

I believe that blood-transfusion becomes safe when supervised by pathologists and technicians who are interested in it and who will spend time and energy on it Such persons can use almost any method with safety

I am glad that I differ so slightly from Mr Evans (Nov 27) in my approach to treatment He admits that it is only in dehydrated patients that treatment with sodium sulphate is likely to be beneficial I submit that it is difficult during the first twelve hours, to differentiate the oliguria of dehydration from that of transfusion nephrosis, and Mr Evans admits that if you make a mistake it will kill the patient since 14 patients of 15 recovered without sodium sulphate, we need more convincing evidence of its benefits For the same reason, I deprecate exchange transfusion, because most patients will recover quite quickly without it

Central Middlesex Hospital
London, N W 10

GEORGE DISCOMBE

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[5] Wiener, A S *J Amer med Ass* 1954 156, 1301

## SERUM TESTS FOR SYPHILIS

SIR,—In your leader of Dec 4 the incidence of specific reactions in the blood transfusion service as 0 04% of sera tested This gratifyingly low surely due to the fact that donors are drawn from young adults, a group in which such reactions expected to be rare The incidence may well be in general hospital laboratories testing sera from with a diversity of clinical conditions

Antenatal sera form a group which may be with blood donors since both represent healthy viduals In recent years at the Whitechapel Laboratory the proportion of antenatal sera positive serological (S T S ) reactions has fluctuated 0 6% but not enough of these have yet been with the treponemal immobilisation (T P I ) test more than very tentative conclusions to be drawn the incidence of non-specific reactions in have carried out T P I tests on 200 antenatal sera to the Venereal Diseases Reference "problem" sera because they had given doubtful S T S reactions in other laboratories these were found to be positive with one or more four S T S used in our laboratory, and of these, 34%, were T P I -negative, suggesting that the reactions were non-specific Although these sera highly selected group, the results suggest that proportion of positive S T S reactions in pregnancy are non-specific may not be negligible, and, in view wide extent of antenatal testing, in the *aggregate* may present a problem of some magnitude It very desirable that the T P I test should be more used to investigate this type of sera, but, for possible, it will have to be established in more than the two already performing it

It should also be stressed that the strength of the reactions is no criterion of their specificity, as the T P I test Although sera giving strongly S T S reactions are usually found to contain antibody, sufficient exceptions occur to make reliance on the S T S titre unwise

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A E WILK

## CORNEAL GRAFTING ACT

SIR,—The increasing numbers of inquiries received from doctors, solicitors, and the general indicate that the provisions of the Corneal Grafting (1952) need further elucidation, especially with to the bequest of donor eyes Briefly, the Act person to make a verbal or written bequest of his eyes for therapeutic purposes but the bequest nullified by the objection of surviving spouse or relative

The collection of donor eyes is the responsibil those who require them, subject to the provisions Act, and collection entails a certain amount of tion and effort in practice, death is usually the hospital by the doctor in attendance or by The duty team then proceeds to collect the taking sterilised enucleation equipment which is maintained in readiness, eyes have to be removed 10 hours of death to be suitable for optical grafts experience these melancholy occasions are treated with a sense of dignity and respect bereaved relatives, who derive consolation fro fact that the last wishes of the deceased are The only occasion on which umbrage has when it was not possible to comply with a because notification of death did not reach the in time and the relatives felt that they had faith

For administration purposes, and to arrange the admission of patients for corneal grafting to ervation of donor eyes has become an essential part his method of treatment At the present time the st suitable method of preservation beyond a few hours o bank the eyes in sterile antibiotic/liquid paraffin tions at 4°C in a refrigerator: such material is able for subsequent grafting up to 14 days after oval provided it is sterile

he sterility of cadaver donor eyes has become a matter reat importance as it has been found that about one d of such eyes have initial contamination by patho ic organisms and have to be discarded This wastage be checked by antibiotic preventive measures at the e of excision or before preservation The eyes or neas are well irrigated with penicillin solution before oval and are immersed in penicillin streptomycin ition before being placed in the eye bank. Control tures are taken at various stages of preparation and servation: a positive culture excludes the use of the for donor material.

n the Corneo Plastic Unit Queen Victoria Hospital, t Grinstead, the supply of donor eyes has been more n doubled since the Corneal Grafting Act became law it is still far from adequate for all purposes The ications of corneal graft surgery continue to expand l the selection of material and cases becomes more l more critical. As a result of these measures and the of improved material the standards of visual success steadily rising and about three quarters of those ients on whom a corneal graft operation is performed y expect improvement of vision in varying degrees to normality A recent valuable adjunct to the final ccess of corneal graft surgery is the use of the contact ses.

t is hoped that this summary may help to answer ie of the many inquiries which are received and it is ased that the collection of this valuable material has n much facilitated by the coöperation of the general titioner house-surgeon relations and ophthalmic geon

ndon, W 1 B W RYCROFT

## CHEMOTHERAPY OF LEPROSY

IR—Dr Lowe is to be congratulated on the good lts he has obtained with sulphones in treating leprosy astern Nigeria (Nov 20), but experience in treating disease in England prompts me to sound a less happy

atients of various nationalities are receiving treatment for omatous leprosy at the Jordan Hospital Earlswood ey they are principally Europeans and Anglo Indians, results with sulphone are unfortunately far from satis ory Although clinical improvement occurs first (thus uraging the patients to persevere with treatment) bacterio al improvement lags sadly behind Furthermore nearly y one of these lepromatous patients receiving sulphone had repeated reactions characterised by fever erythema sum neuritis arthralgia, and mental depression. The *essful management of such cases calls for considerable* cal experience.

feel sure that Dr Lowe would be the last to say that iks to sulphones all is well in the therapy of leprosy, the average reader of his paper may have gained the ression that the disease has finally been mastered rying to find an explanation for Dr Lowe s encourag results one must take into consideration the fact the leprosy situation in Eastern Nigeria is particu favourable for the disease has largely been brought er control by the system of clan segregation which instituted some twenty or more years ago This has ed the lepromatous rate to fall considerably leaving portionately fewer advanced lepromatous cases

his letter is written not to belittle the excellent work astern Nigeria but to dispel any attitude of com ency which Dr Lowe s paper may have engendered to warn readers that his results apply to Africans in a particularly well favoured part of Africa and are exceptional We have a long way to go in the treatment of leprosy and the need for more research into newer and better methods of treatment is vital and urgent

Hospital for Tropical Diseases
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W H JOPLING

## PULMONARY EMBOLISM

SIR,—Your leading article of Jan 1 is timely in drawing attention to a much neglected cause of prolongation of invalidism and of a steady mortality among the middle aged and elderly

Thrombosis of the deep veins of the leg in elderly patients is commoner that many of us imagine If post-mortem figures are to be relied on, Hunter et al.[1] have shown that thrombosis of the deep veins is present in 52 7% of middle-aged and elderly patients confined to bed They also found that these thromboses are relatively silent until the unheralded catastrophe of a massive pulmonary embolus. In a series of post-mortems performed by myself in the past few years massive pulmonary embolism was the immediate cause of 20 (4·4%) deaths out of 448 In 18 of these cases the catastrophe followed on operation or accident

It seems that present-day preventive measures have failed Israel[2] affirms that great attention has been given to prevention of venous thrombosis by employment of early ambulation prophylactic femoral vein ligation and the use of anticoagulants. It is disappointing that studies indicate no reduction in frequency in thrombo-embolism has been achieved.

There is some evidence both clinical and laboratory that too much fat in the diet predisposes to clotting Fullerton et al[3] have shown that after a large fatty meal the prothrombin and clotting times are greatly reduced compared with the fasting times Other workers[4] have shown that a lipoid factor is essential for normal clotting but its precise character has not been determined

From the clinical aspect Dedichen et al.[5] have shown that in Norway the incidence of thrombo-embolic phenomena after operations liable to cause such complications fell very markedly during the German occupation They believe this was due to the reduced diet especially of fat the calorie intake fell from 3470 to 2840 per day and the fat intake from 159 to 71 g per day In Denmark, during the same period rationing was not severe and the incidence of thrombo-embolic phenomena continued as before

In view of the failure of present-day preventive methods it might be worth arranging a large inquiry to show whether a light low fat diet in the days after operation or trauma might not reduce the death rate and invalidism from pulmonary embolism

Worthing Hospital
Sussex

R AIDIN

## REPAIR OF FEMORAL HERNIA

SIR,—In his letter of Dec 18 Mr Sandell makes a useful suggestion for the reduction of the sac in femoral hernia, but I notice that he advocates the Lotheissen operation Surely the method of McEvedy is to be preferred? And better than either in my opinion is the approach through a lower paramedian incision without opening the peritoneal cavity I have used this approach routinely since 1948 and find it extremely satisfactory but I have met few registrars or house surgeons who have seen it used

The rectus muscle is retracted to the appropriate side and with gauze—or better still with the fingers—the fascia in the hypogastrium and iliac fossa is gently swept backwards. The upper surface of Gimbernat s ligament can then be seen together with the disposition of the obturator vessels and the bladder Further gauze dissection exposes the hernia and one can usually predict the contents of the sac from its appearance and from the history With gentle pressure

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1 Hunter W C., Sneeden V D Robertson, T D Snyder G A C. *Arch intern Med* 1941 68, 1
2 Israel H L. *Postgrad med J* 1953 13 9
3. Fullerton, H W., Davie W J A., Anastasopoulos G *Brit med J* 1953 ii [illegible]
4 Macfarlane, R. G *J Physiol* 1941 99 7
5 Dedichen, J Strom, A., Adelsten-Jensen, R. Transactions of 5th Conference Josiah Macy, Jun, Foundation, New 1951

Dr. Robert Heilig

below Poupart's ligament, and very gentle traction on the sac with gauze, judicious blunt dissection delivers the sac without cutting The most adherent part seems often to be in front, and there may be delay in freeing the sac from the deep aspect of Poupart's ligament—which is, however, clearly visible

The peritoneal cavity can, of course, be opened if, for any reason, that seems the safer method

I consider it unnecessary to close the upper end of the femoral canal, but this can be done easily by stitching Poupart's to Cooper's ligament As a rule there is remarkably little bleeding, and I have never seen a hæmatoma form in the thigh.

Familiarity with the space through which the operation is done is valuable, for it is the best approach to the prostate, a large portion of the bladder, the lower ends of both ureters, the obturator nerves, the proximal ends of the inguinal and femoral canals, the spermatic cords, and the external iliac vessels and lymph nodes The appendix and the female genitalia are also accessible if the peritoneal opening, made when the inguinal or femoral sac is cut off, is slightly enlarged , and it may be wiser to remove the appendix if there is anything odd about the pain ascribed to a right sided hernia

Harrogate T VIBERT PEARCE

## SYME'S AMPUTATION

SIR,—It would indeed be unfortunate if, following Mr Shelswell's article of Dec 25, the profession were induced to try again Syme's amputation, which was relegated to the surgical scrap-heap thirty years ago, and if the lessons, so slowly and painfully acquired during and after the 1914–18 war, had to be learnt once again Soon after that war, the surgeons at Queen Mary's Hospital, Roehampton, of whom I was one, undertook a long and thorough review of Syme's amputation, in all its aspects I would emphasise that this review was done with absolute impartiality and we had no brief from either the detractors or the sponsors of the amputation, though the latter were far the more vocal Our findings were very definitely against the amputation, and in consequence it was accepted by surgeons, in this country, as obsolete Our reasons for condemning Syme's amputation were

(1) Less than 40% of the original Syme's amputations under review had been capable of taking full end bearing Most of the cases unable to take full end bearing had had reamputation through the middle third of the leg and the vast majority of these reamputees had expressed the opinion that their efficiency had been increased, in greater or lesser degree

(2) Secondary operations on the stumps of Syme s amputees —e g , excision of scars, neuromata, &c —were almost invariably " failures "

(3) The amputation was quite unsuitable, for æsthetic reasons, in women For the same reason, though to a much lesser degree, it was undesirable in men

(4) The prosthesis for a Syme's amputation necessitated a leather socket which is not as comfortable as willow or duralumin Further, the leather socket has other disadvantages —e g , smell, prevention of evaporation of sweat, &c

(5) The " wear and tear " of a Syme's prosthesis was much greater than of the ordinary below knee leg

(6) The gait of the Syme amputee, with his prosthesis, was ungainly as compared with the below knee amputee

(7) The functional efficiency of the below knee amputee, with a good stump, was slightly better than that of the satisfactory Syme amputee

Perhaps our greatest difficulty in persuading the sponsors of Syme's amputation of its unsuitability was to convince them that, although the stump which they had fashioned so admirably might appear so wonderful to them, this was really no criterion at all

If the matter is pursued, no doubt we will again have the old arguments adduced that the limb maker should make his prosthesis for the stump, not the the stump for the prosthesis , that many of the original Syme's amputations were faulty because technique, or that they were done with improper tions (e g , frostbite) , that the stump which ca full end bearing must be the ideal stump , that Syme's prosthesis is cheaper than the below kne thesis , and so on All these arguments were ca considered by us at the time, but we were in no about our final judgment against the Syme

The fallacy of Mr Shelswell's investigations he has taken the residual " less than 40% " sati Syme's amputees and has proved that 66% of th satisfactory This means that about 26% of the Syme's amputations continue to be satisfactory— a reason for resuscitating a discredited operation.

Croydon G C WELL

## TRANSHEPATIC CHOLANGIOGRAPH

SIR,—The Association of Surgeons at its mee Glasgow next April is to discuss diagnostic proc in obstructive jaundice I have been asked to c information about preoperative transhepatic chol graphy—a procedure not often carried out—and I be grateful if any of your readers who have had *ence of it would let me have a brief account* of results, including particularly any complication

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DAVID H PA

## MERIT AWARDS

SIR,—The M D B circular no 19, concerning proportion of distinction awards payable to c teachers and research-workers holding honorary ap ments, to which you referred briefly on Dec 25 (p must restrict the scope of research that is to be taken by such men The fraction of the award no paid is to be based upon the number of hours sp strictly clinical work, and time spent upon resea to receive financial reward only if it is " spec related to the diagnosis and treatment of indi patients " (my italics of an important word which omitted in your report) This restriction on the pa of distinction awards gives whole time clinical re workers a financial incentive to neglect the deve of new diagnostic or therapeutic measures which first be studied at the laboratory bench or upon They will only be paid the whole of any award t they are entitled if they either restrict their well established procedures or if they try out t *operation*, the *new drug*, the *new catheter*, an directly upon patients even though preliminary tory study is necessary ! Nor can these res consider any extension of their interests into pre medicine without financial loss The man, for who tries out well-known palliative treatment victims of smog will get his award in full, but man who decides to investigate the effects of atmospheric pollutants on the respiratory tract to guide preventive measures, or even to dev efficient respirator to protect individuals befo become patients

Distinction awards were, of course, originally duced as a recompense for the loss of income from practice which consultants in the N H S were e to suffer, so that it is logical to allocate them in to time spent in clinical work , but this is da logic, and the decision to make whole time ac clinicians fully eligible for the awards was a pro step towards the recognition that those who cult tree of clinical science deserve at least as great as those who garner its fruits The new regulat retrograde step, and if it is strictly applied it mu harmful influence upon the development of research in this country

Richmond Green,
Surrey

C M FLE

## CURRENCY FOR TREATMENT ABROAD

IR —Since the war it has been necessary to restrict use of British currency abroad and seven years ago Exchange Control Medical Advisory Committee was up to deal with applications by patients advised to medical treatment overseas No one in the Govern t or otherwise liked the idea of restricting facilities l for health and the responsibility of allocating ign exchange on medical grounds was entrusted to a lical committee with the duty to safeguard the rests of the patients, as well as conserve so far as sible our limited foreign exchange

t is the Government s policy to simplify exchange trol procedure and in future the patient s bank will authorised to grant foreign currency solely on the ngth of a doctor's recommendation that it is required medical grounds Banks will provide a printed n but the doctor may write his own certificate vided similar wording is used

When currency is required for the United States of erica or Canada, the patient s doctor will be asked to ify that the dollars are required for medical or gical treatment which cannot be obtained elsewhere

he Exchange Control Medical Advisory Committee ld like to take this opportunity of thanking their lical colleagues all over the country for their patience forbearance The doctor has generally had the cate responsibility of deciding whether he ought to port a patient s desire to go overseas or whether tment at home would be equally satisfactory lging applications has not been easy but the committee happy to think that even in the most stringent ncial period over 75% of applications were granted, during most of the committee s existence more than Few if any sick people in genuine need of treatment h could not be obtained in this country or the ling area have been unable to obtain it

xchange Control Medical
Advisory Committee
Tavistock Square
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HARLEY WILLIAMS
Secretary

## VENEREOLOGY AND DERMATOLOGY

R —Mr King and Dr Russell (Jan 1) consider the nt advertisement of a combined post in venereology dermatology to be a retrograde step I would like omment because I worked in that East Kent area n 1938 to 1946 and also because I happen to be one he few consultants permitted to practise both alties since the National Health Service began

e incidence of venereal disease in East Kent would nsufficient to hold the interest of a venereologist s he were also attached to a larger centre and my own experience that entails a great deal of elling and waste of time Furthermore clinical rial and facilities for research—the life blood of mbitious specialist—are not always available in a rural area but many good clinicians do not aspire is

principle I am in favour of the separation of these alties although in many parts of the world they are combined We should however guard against too n specialisation : there is still room for the general eon and consultant physician as distinct from the alist there are difficult cases where the broader is sometimes of value A special knowledge of atology is often useful to the venereologist and versa secondary syphilis has been diagnosed as onamide rash by a dermatologist and psoriasis een unrecognised by a venereologist

ny consultants have a competent knowledge of both lties My senior registrar in venereology holding a joint ntment with another hospital (I understand he is not plicant for the post in question) has, as a result of the suggestion of a ' pure dermatologist at the selection committee also worked regularly for three years in the skin departments of both hospitals

However good the separation of these subjects is in principle there are exceptions to every rule and the conditions in East Kent are in my opinion an example of one such instance It is surely better to offer the right man adequate employment so that both specialties are adequately covered than to appoint two men who might stagnate and find outside interests Some specialists give much time to committee work or politics I fail to see why utilising this spare time in another medical interest is a retrograde step

London W 1

DAVID ERSKINE

## MEDICINE IN THE SOVIET UNION

SIR —Dr Fox s broadcast not only raised points of interest with regard to upbringing and its results in the U S S R but also invites comparison between planned methods of training of children and our own laissez faire It may be profitable to consider further the three types of community to which Dr Soddy refers in his letter of Dec 25

Neurosis, in all its manifestations has a double origin It arises first from unresolved dissatisfaction in the early parent-child relationship but its second cause equally important is the strain put on the individual by the outside world which makes demands different from his expectations Fear and dissatisfaction then work on his inner structure and produce the symptoms

In the wholly planned community the first emotional relationship is likely to be different from ours only in so far as the parents may have more economic security though perhaps if the individual fits the ideal picture prevalent in that culture he will have special reason to feel confident Any deficiencies in this early relationship however may never become manifest because of the continuity in the framework within which the individual lives From the earliest age conformity is demanded and security given in return The love instincts may or may not be satisfied but the child s hate is distributed on to others ' whom he may indeed be required to hate Provided he is no rebel—and the large majority of humans are conformists—he need not come into conflict with an outside world which differs from his expectations and he is thereby saved from neurosis.

In the type of community the U S A represents the child is reared at first in an intensely individual atmosphere This is followed (as Dr Soddy points out) by an equally intense training in group relationship and loyalties Finally he enters a fiercely competitive workaday world which brings him into conflict both with his early ethical teaching and with his group identifications This conflict is the crux of the tension and anxiety which is produced

In our type of morality the bonds are intense at first, but the group does not wholly replace family influence nor is the adult world based entirely on competitive success values Nevertheless the individual has almost always had an imperfect relationship in the home and the very looseness of the bonds and the variety of choices and expectations are also likely to induce conflict There is a crisis aspect of childbirth—partly economic—which evokes anxiety in many homes. This is transmitted to the child as well as the uncertainties caused by the absence of a stable broad synthesis. Very few people are able to achieve such a synthesis by the time they are physically fit and able to have children

During the last 50–70 years our larger ethical framework has collapsed and its collapse has deprived us of pegs on which to hang our standards. It has also led to a piecemeal revision of our methods of upbringing and education which has put a very great strain on the individual Though we have advanced beyond the stage where a ready-made pattern, of supposedly universal validity, would satisfy us, we are far from giving the individual the strength he needs to enable him to get satisfaction from his world, nor have we tried to remove inconsistencies from his thorny path, or prepared him from his childhood onwards to meet the world's expectations to the best of his ability To my mind, this is the explanation of our higher breakdown-rate, which is therefore to some extent preventable As a nation we are, in the eyes of the outside world, rather more secure than we have been for some time past, and it is now up to us to fit the individual better for his task In particular, we must enable him to grow up better equipped emotionally and to have continuity in the demands made on him

Roehampton, London, S W 15 HEDY SYMONDS

## BED-WEIGHING MACHINE

SIR,—In work on changes in metabolism of water and electrolytes after injury we were concerned with obtaining accurate daily weights of patients, most of whom were bedridden and some of whom were being treated with Sinclair traction apparatus There was at that time no suitable bed-weighing machine in this country, though a Swedish model had been described [1], so, while awaiting completion of the Avery (33N) machine described by Darmady,[2] we experimented with a modification of a personal weighing-machine

A steel trough was attached to the platform to accommodate the two castors of one end of a hospital bed so that each end of the bed could be weighed separately, the end not being weighed was raised with wooden blocks to the level of the platform The accuracy of this method —and later that of the bed-weighing machine (type 33N)—was tested by repeated weighing of beds with and without occupants When satisfactory techniques had been established, different patients and beds, with and without Sinclair traction apparatus, were weighed With both methods of weighing, the beds were lowered to the ground after each observation, in this way each bed was weighed ten times The accompanying table summarises the results and gives the standard deviations calculated from the serial weighings

The improvised method was found to be insufficiently accurate for following daily changes in the balance of water, but the bed-weighing machine proved entirely satisfactory for this purpose It will be seen from the table that with the bed-weighing machine the error is virtually independent of the absolute weight being measured, and that changes of more than about 50 g based on single readings have less than a 5% chance of being due to error in weighing Greater accuracy be obtained if on each occasion the mean of weighings is taken

| Method | Mean of ten weighings (kg) | | | Standard error (g) | |
|---|---|---|---|---|---|
| | Mean total weight | Bed only | Patient only | Single observation | Mean of ten weighings |
| Improvised bed weighing machine | 144 790<br>151 750<br>146 400<br>206 680<br>90 375<br>81 720<br>75 670<br>68 760 | 90 430<br>90·540<br>90 355<br>140 030<br>90 375<br>81 720<br>75 676<br>68 760 | 54 360<br>61 210<br>56 045<br>66 650 | ± 2896<br>± 3280<br>± 3260<br>± 2599<br>± 1616<br>± 1961<br>± 1835<br>± 1629 | ± 916 4<br>±1038 5<br>±1031 9<br>± 822 1<br>± 511 4<br>± 620 6<br>± 580 8<br>± 515 0 |
| New bed-weighing machine (type 33N) | 192 266<br>126 544<br>191 076<br>227 680<br>146 142<br>78 805<br>82 644<br>72 544 | 123 486<br>65 284<br>121 026<br>122 260<br>78 805<br>78 805<br>82 644<br>72 544 | 68 780<br>61 260<br>70 050<br>65 420<br>67 337 | ± 23 1<br>± 27 2<br>± 27 8<br>± 16 8<br>± 27 8<br>± 22 8<br>± 16 8<br>± 16 8 | ± 7 3<br>± 8 6<br>± 8 8<br>± 5 3<br>± 8 8<br>± 7 2<br>± 5 3<br>± 5 3 |

Birmingham Accident Hospital C T G Fr

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[1] Alwall N *Acta med scand* 1952, 143, 158

[2] Darmady E M *Lancet* 1954 ii 680

## RENAL CHANGES IN ECLAMPSIA

SIR,—As a survey, your annotation of Dec. disappointing because it fails (a) to take acc the researches of Oliver [1] and Sheehan [2], (b) to re that the release of thromboplastin cannot be an es ætiological factor in eclampsia, (c) to relate G findings to similar findings in cases of hyperte (d) to weigh the evidence which denies the a corticoids a *primary* ætiological importance, and appreciate the rationale of modern therapeutic n

In Oliver's *original investigation* on the kidneys by Shaw Dunn [3] *from cases of obstetric* anuria ( eclampsia), considerable necrosis of the renal cortex, survival of the juxtamedullary area, was apparent Wh nephron dissection was *undertaken, the damage* appe be due to an altered vascular state rather than to a Sheehan's extensive series of anuric (including post-e kidneys showed lesions which *could only have* been spasm of the intralobular arteries Thus both thes attribute the renal condition to ischæmia

McManus [4] says that in acute hypertension the arteries of interlobar size "show a marked thickening intima in a concentric laminated fashion" The gl shows proliferation of epithelium and endothelium, wit proliferated epithelial cells of the visceral layer bec filled with large colloid droplets, and the tubules are d and lined by enlarged cells full of colloid droplets C notes that in eclampsia the afferent glomerular artery eccentric subendothelial deposits, there is increased larity of the glomerular tufts with formation of droplets intercapillary space, and the proximal convoluted show cloudy swelling and contain albuminoid débris ing for differences in interpretation, both these author to be describing much the same condition If in McM cases this was known to be the result of a raised blood why should it be attributed to a different cause in C

There is no evidence that in the 12 pregnant w Govan's series who were free from eclampsia, or renal disease the renal vessels had not during p been subjected to hypertensive factors which had rai pressure above its pre pregnancy level

As adrenocorticoids have not been demonstrated to in amount pari passu with the increase in toxæmia— they actually decrease as pre eclampsia mounts unlikely that they are primarily responsible for the *manifestations Moreover the potassium loss pro* adrenocorticoids, accompanying sodium retention, is in pregnancy toxæmia [6] To induce hypertension the *corticoids require a great excess of sodium,* and prophylactic restriction of salt should—at least in th deprive them of such an effect No hormonal hyp could explain why the primigravid are peculiarly eclampsia The toxæmia like effects which you men having been produced in rats by injection of posterior p extract could well be due to renal ischæmia, which h shown to occur by Trueta et al.[7], for, in rats deoxycortone and sodium chloride,[8] similar effects res injection of renin—a substance proved to provoke ischæmia.[9] Byrom [10] also has produced an eclamp state in rats by inducing renal ischæmia with the Go clamp

*It* is renal ischæmia that the experimental, clin pathological evidence incriminates, and the ther lence points in the same direction The success obtained hypotensive drugs can be explained by their increasing l blood-flow Likewise dramatic improvement in mpsia occurs when conduction anæsthesia reaches the l of the lesser splanchnic nerve[11] thereby reducing the vous impulses responsible for renal ischæmia

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[1] Oliver J, Macdowell M, Tracy, A *J clin* 30 1305

[2] Sheehan H L Moore H C Renal Cortical Necrosis Kidney of Concealed Accidental Hæmorrhage Ox

[3] Shaw Dunn J Montgomery, G L *J Path Bact* 19

[4] McManus J F A Medical Diseases of the Kidney 1950

[5] Venning E H Singer, B Simpson G A *Amer J Gynec.* 1954 67 542

[6] See *Lancet* 1953 ii, 121

[7] Trueta J Barclay, A E, Franklin K J, Daniel, Prichard, M M L Studies of the Renal Circulation. 1947

[8] Daniel P M Prichard, M M L, Ward McQuaid J *Physiol* 1954 124 106

[9] Gaunt R Renzl A A *Ciba Symp* 1954, 6, 1

[10] Byrom, F B *Lancet* 1954 ii, 201

n your leader on anuria (Dec 11) you have equally rlooked the ætiological significance of the spasm of renal cortical vessels although you have indicated its dence in the four clinical types described. This ulatory change in anuria has been combated very cessfully by the Dublin school of obstetricians in way which incidentally elucidates the pathological nges responsible for anuria Over the past two years Feeney[12] and Dr Barry[13] have demonstrated the ue of splanchnic block in incipient and early estab led anuria complicating concealed accidental hæmor ge (which you recognise as the most formidable com ation of circumstances) They have also lent support my thesis by recording improvement following rupture the membranes in that condition

It will soon I believe be clearly evident that eclampsia d the anuria it produces, are the result of a renal tical ischæmia provoked by the resistance of the rometrium to stretch

ondon W 1  JOHN SOPHIAN

## MENTAL CHANGES AND ORGANIC DISEASE

SIR,—I have read with interest your annotation of v 13 on this subject.

I would point out that we did not say that the ychiatric diagnosis was abandoned after localised normalities had been found in electro-encephalograms ther we wished to emphasise the presence of an ganic lesion in addition to the psychiatric difficulty e were and continue to be concerned about the nbers of patients who do have organic disorders of central nervous system and in whom the presenting ptoms are primarily psychiatric

am unable to understand the last phrase of your ment ' *but its routine use as recommended by* ggoner and Bagchi is likely to give rise to other gnostic mistakes ' Certainly this is not a valid ment if the electro-encephalogram and clinical studies properly evaluated

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University Hospital
Ann Arbor
Michigan U.S.A  RAYMOND W WAGGONER.

* It was the likelihood that routine use of electro- phalography in mental hospitals might *not* always accompanied by adequate evaluation of clinical and tro encephalographic studies that gave rise to our ment —ED L

## REACTIONS TO IODISED OIL

IR,—For thirty years almost every week I have doing hysterosalpingograms probably well over ) In 90% of these iodised oil has been used in water-soluble dyes In my own mind I have no bt that the advantages obtained in the 90% from point of view of diagnosis and therapeusis have outweighed the very small risk of experimental ulomata referred to by Mr de Boer in your issue of 25—a condition which I am prepared to admit it occur if the tube be obstructed at the fimbria mpulla But should a tube be found so pathologically ed using either solution I would remind him that chances of surgical success or natural recuperation certainly under 15% Moreover he will readily l that it is the very commonest of surgical findings e the convolutions of a small tortuous hydrosalpinx closely adherent and kinked—properties of minor obstruction by no means solely confined to the oviduct of Fallopius

Those who run fertility clinics are generally agreed that after an intimate history has been taken a Rubins $CO_2$ test is the first line of investigation. Only should this be doubtful or negative is recourse had to an oil test for if there is no clinical question or palpable doubt that the case is one of primary sterility or for that matter a clean case of secondary sterility then I am confident that iodised oil used gently and meagrely under the keen screen control of a radiologist, is best Moreover in such a case I believe it is just because of the nascent iodine that such a technique is so often of great therapeutic value for it is quite phenomenal to see and hear of the number of patients who have conceived immediately after the use of iodised oil If however there is a history (not so very common these days) of tubal infection or febrile salpingitis there is perhaps some reason for the use of water soluble radio opaque material, though even here the transient fluffy smog like shadows, at the end of the tubes are often difficult to interpret On many occasions when such cases have failed to conceive or have undergone further investigation it has been shown at laparotomy that the tube so happily diagnosed as patent because of an immediate fog of material at its end is in reality a tube and ovary surrounded by mosquito-curtain like veils of peritoneum absolutely inhibiting exit or entry of the ovum.

At the Royal Society of Medicine I was speaking of cornual occlusion of the tube secondary either to criminal abortion, induced abortion or postpartum infection Repeated $CO_2$ and oil tests demonstrate that in 95% of patients giving such clinical histories where there is no palpable abnormality whatever the blockage is never beyond the isthmus but confined to the cornu and interstitial portion of the tubes

In such cases there is no question whatever that a clean-cut iodised-oil picture is an essential prerequisite to surgical intervention subsequent operation always demonstrating that the distal portion of the tube is abolutely healthy and therefore readily implantable Such a picture can never be obtained by the usual hazy dyes, though the new material Salpix may prove to be the exception

London W 1  V B GREEN ARMYTAGE

## RECOGNITION OF TABLETS

SIR —Manufacturers might use a system of code numbers to help doctors to identify by sight those tablets they have previously prescribed A simple system of duplicate records might however prove less unwieldy in the long run It would be virtually impossible to carry any code beyond the range of the proprietary tablets To consider the extreme case hospitals now often compress certain tablets to meet their own needs specially made punches and dies would certainly not be forthcoming to codify such tablets Moreover an established drug (for example phenytoin sodium) will often masquerade as a plain tablet marked tablet sugar-coated tablet or capsule In such circumstances the only sure guide is chemical identification

The scheme of identification I have outlined[1] has been elaborated to meet the needs of a busy hospital, and has proved perfectly workable It is quite true that time care and some apparatus are required for the tests—especially care But although the reagents are unstable the components may be stored for a month or more without prejudice to the reactions Fresh reagents are an important safeguard against false negatives which would be very misleading Compound tablets are not quite so baffling as you suggest in your annotation of Jan 1 The main toxic ingredient can be detected almost invariably within the ten minutes allowed and the rest of the tablet can then be investigated at greater leisure As in any simplified scheme there are notable

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llington R A *Curr Res Anesth* 1947 26 238.
eeney K J *J Irish med Ass* 1953, 32 36
arry A J Geoghegan F *Irish J med Sci* May 1954 p. 189

[1] Cooper P *Pharm. J* 1954 173 481

lacunæ, for instance, there is no rapid test for the presence of the amphetamine series Much work remains to be done on the lines suggested in my preliminary investigation Meanwhile I would urge that casualty-officers suggest to their hospital pharmacist that a chemical identification service be available for any real or suspected poisoning emergency Where a hospital has no pharmacist, the coöperation of a local chemist might be enlisted

Pharmaceutical Department
Southmead Hospital Bristol
PETER COOPER

SIR,—We were interested in your suggestion that manufacturers should consider stamping tablets with code numbers It has long been our practice, and we believe also of some other companies in the industry, to emboss tablets with a distinctive mark A list of our tablet markings is available on request to any doctor who would like to have it

There is a feeling amongst some pharmacists that it would be better if tablets were more uniform in size, shape, and colour and if sugar coated tablets, for instance, were all white Whilst we believe this might have some advantages to the retail pharmacist, we think it would be less convenient to the medical practitioner Apart from the urgent problem of identifying a possible cause of poisoning, there are many other occasions when it is useful for a doctor to look at a tablet and to be able to immediately identify it by a mark or other characteristic with which he is familiar

Bayer Products Ltd
Kingston on Thames
Surrey
L M SPALTON
Director

## AGAMMAGLOBULINÆMIA

SIR,—I hesitate to prolong this discussion, but I feel I must correct one or two statements made by Dr Bowley and Mr Dunsford in their letter of Dec 11

They state that no query would have arisen had I advised Dr Grant and Dr Wallace that I had used βα in the examination of the group Yet I did say that Dr Grant and Dr Wallace used only part of my report I had, of course, advised them of my investigation, but they had every right to make use of my report in part or in full, as they thought fit They emphasised the pathological and clinical aspects of the case, because these were of more general interest than the serological investigations I assumed (as it turned out, wrongly) that my colleagues would realise that where blood grouping is performed on many thousands of samples, it is usually done by people who know something of the subject I am pleased that my findings are now acceptable

I was not in fact surprised when we found α missing I suspected some serological abnormalities when Dr Grant first presented the case at a local scientific meeting, and I therefore asked permission to perform the serological investigation I am sure Dr Bowley and Mr Dunsford are very familiar with the extensive literature on the location of the β and α agglutinins in the plasma, so they will know that these two agglutinins are located in the gamma fraction [1] I am therefore certain that had they been presented with such a clear-cut case of agammaglobulinæmia, they would not have been surprised at finding serological abnormalities

Concerning secretion of group-A substance, I did know of the paper by van Loghem [2] to which Dr Bowley and Mr Dunsford refer, what I said was not that I could not find any paper which showed that people of these subgroups of A did not secrete group A substance, but that "I was not able to find any literature supporting their dogmatic statement" The paper by Grove-Rasmussen et al [3] (which they themselves quote) says that the saliva of the donor K7332 inhibited group O serum when this was tested against his own cells which surely means that the donor secreted in his saliva something which, Dr Bowley and Mr Dunsford must admit, behaves very much like group A substance

In their last paragraph they say "A study of th
will show there are marked differences between A$_4$ and
Undoubtedly the literature must be studied, but
scientist should read with discrimination Uncritical
tance of everything published often creates confus
confounded I think they will agree that we have had
of confused terminology in hæmatoserology, and I therefore refer them to some parts of the literature where
differences do not appear so very marked For ins
Grove Rasmussen et al [3] say "Dunsford refers to a
blood studied by Gamelgaard and Marcussen but app
term A$_4$ for this type of blood The term A$_0$, however
preferable because it is more descriptive of its
behaviour with Group O serums " Again, Race and
in their latest edition of *Blood Groups in Man* say (p
"van Loghem and van der Hart have found thr
(*synonyms $A_x$ and $A_0$*) children " (*my italics*)

All this has really nothing to do with the
paper by Dr Grant and Dr Wallace, and I hope
Dr Bowley and Mr Dunsford will agree that
controversy should now end

Birmingham
W WEL

## SHOE DESIGN AND TOE DEFORMATIO

SIR,—Professor Haines and Mr McDougall (Dec 25)
further proof of the bad design of the footwear of
adult and adolescent They rightly state that "Ideal
pressure on the toes should be avoided" and it is
cant that it is always this feature of design that i
first to be modified or abandoned *Satra Bul*
reporting on the adoption of their "ideally" de
lasts for children, comments [1] that "several firms
adopted lasts modelled by us Others have re
minor modifications, especially in toe shape."

Professor Haines and Mr McDougall may be wrong
they say that "the modern male track runners' spiked
has to be somewhat pointed and very tight over the
give the grip required" It may indeed be designed
way and these features may be essential to "fit" that
of footwear, but, I submit, shoes for this purpose
accommodate the feet so that they function as natural
as efficiently as possible Observe the feet on the
runner and you will find he seeks the maximum
contact for his toes, thereby getting the best possible
As I have suggested elsewhere,[2] shoes designed on the
by adding to the efficiency of the feet might well knock
off track records

Professor Haines and Mr McDougall also state "th
design of most shoes for adults "must necessarily d
however well fitted." This statement will appear
dictory to many readers who believe, as I do, that you
"fit" a badly designed shoe The term "fit," howev
become so ambiguous and so widely used by the
of shoe reform that its use is dangerous and its m
capable of gross distortion

All foot surveys to date have carefully avoided
consideration of shoe design all faults of design
been included in the classification "a short fit" or
fitting"—which are both terms implying that th
no fault of design but faults of selection by pur
or retailer

This of itself may not seem important but, as I
already shown,[3] such things affect Government
and a study of the latest report from the Min
Education [4] confirms this view In support
complacent attitude the Ministry quotes twice
page references to reports stating there is no corr
between foot deformity and shoe fitting There
mention of shoe design nor of the fact that it is imp
to obtain factory-made shoes that will not deform
of school leaving age No doubt many parents
delighted to hear the news given in the report th

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1 Payne R., Deming Q B *J Immunol* 1954, 73, 81
2 Vox Sang 1954, 4, 69
3 Grove Rasmussen M, Soutter L, Levine P *Amer J clin Path* 1952 12 1157

1 *Satra Bulletin* January 1954 vol 6
2 *J All Nations Sports Ass* 1953, 5 5
3 *Lancet*, 1953 ii, 143
4 The Health of the School Child H M Stationery Off

h of the country s children was everywhere satis ory but those of us interested in children's feet no grounds for satisfaction and we deplore the ent attitude of the Government

present no factory made shoes are available for ts or adolescents that avoid all pressure on the ' The shoes available are not only producing much rmity but also preventing correction of existing rmities Surely this is a matter requiring the urgent ation of the Minister of Health

ndon S E 15 CHARLES A PRATT

R —Having advocated a straight inner border to otect the great toe from excessive deviation Professor nes and Mr McDougall add but unless other stments were made to resist it the pressure on lateral toes would be unbearable" It may be d

Is not any deviation of the great toe excessive ?

Why if the shoe is designed to fit the foot, and pressure fore taken on the heel and instep should it be assumed there is any pressure on the lateral toes—let alone an arable one ?

Surely in the sentence containing the words "the bad n of most shoes for adults" *all* should be substituted for ?

ndon W 8 G G SHERRIFF

## PTIC ULCERATION IN SOUTHERN NIGERIA

R,—The article by Mr Konstam in your issue of 20 was of particular interest to me since I have ated on 16 cases of acquired pyloric stenosis in ans living in the south-east province of Sierra Leone e past two years All gave a long history of epigastric with symptoms of advancing pyloric stenosis and e majority the stomach was huge—even in a boy who was the youngest in my series. All were treated astrojejunostomy except one on whom partial ectomy was performed

their clinical features and the striking success of e operative measures my cases closely resemble the scribed by Mr Konstam But my operative findings significantly In all my patients there has been a loric mass of granulomatous tissue often ulcerated o centre Smears taken from the surface of this shown the ova of *Schistosoma hæmatobium* in nearly the cases and the appearance has resembled the ror of the urinary bladder in advanced bilharzia of organ Mr Konstam s cases revealed a state of ic duodenal ulceration with extensive adhesions d My experience has also been that adhesions ery dense and extensive and involve the pylorus luodenum with neighbouring organs On several ions I have found *S hæmatobium* ova in these ions and in the free peritoneal fluid There is a *resemblance between the adhesions found in this* ion and those seen in bilharzia of the female organs

istosomiasis is hyperendemic in this region the e being either active or latent in almost all the ation from the age of five or even younger onwards uspect that infestation with hæmatobium (far from ing its clinical manifestations to the urinary tract) both widespread and serious lesions in many parts body From the few cases of pyloric stenosis I so far treated it is impossible to draw conclusions is perhaps permissible to suggest that this con —in this country—is often a late result of a heavy ation with hæmatobium It would be interesting to whether this or other helminths commonly invade all of the stomach in the people of Southern a

ethodist Hospital
rema, Sierra Leone. J R ROSE

# Obituary

## CHARLES JENNINGS MARSHALL

M.S M D Lond., F R C.S

Mr Jennings Marshall senior surgeon to Charing Cross Hospital died at his home in London on Dec. 29 at the age of 64

The son of C W Marshall, he was born in Cardiff and was educated at Cardiff High School. From Charing Cross Hospital Medical School he graduated M.B with honours in 1912 and was awarded the gold medal of the University of London After holding house-appointments at Charing Cross he took his M D in 1914, and while holding the post of surgical registrar the F R C.S. in 1915 The following year he gained the degree of M.S and again carried off a gold medal

The same year he accompanied his former chief Sir Herbert Waterhouse to Petrograd to join the staff of the Anglo-Russian Hospital which had been set up as a gesture of good will to our allies. Jennings Marshall served the hospital as assistant surgeon, and on his return from Russia he joined the R.A M C and was posted to Salonika

After the war he became assistant surgeon and junior orthopædist at King s College Hospital, but he gave up this appointment when he was elected to the staff of his own hospital He also joined the staff of the Victoria Hospital for Children, Tite Street where he had charge of the orthopædic department For many years he was a surgical consultant to the Ministry of Pensions and to the London County Council, He was an examiner for the universities of London and Manchester During the late war he was director of the surgical section of the Sutton Emergency Hospital

As a surgeon his interests and his experience were wide After the 1914–18 war he continued his work in orthopædics, notably at King s and at Tite Street, and in 1921 he described in our columns with verve and insight the arm training centre at Roehampton But he was in fact a general surgeon Though his monograph in 1938 was entitled *Chronic Diseases of the Abdomen* he pointed out that in his view the abdomen extends at least from the knees to the eyebrows. The racy style based on shrewd observation was typical of his teaching and his practice His other writings in collaboration with colleagues include *Textbook of Surgical Pathology* and *Textbook of Surgical Anatomy and Physiology* He wrote less than he might have but many of his unpublished practical innovations will live in the practice of his students. His friends at the Savage Club will also recall his self made receiving-sets in the early days of wireless, and his delight in music and the arts.

Mr Jennings Marshall married Miss Hope Embleton Smith who survives him

## HARALD NORRIS WEBBER

M.A., B Chir Camb F F.A R.C.S

Dr H N Webber consulting anæsthetist to University College Hospital, died in London on Dec 24 at the age of 73

The elder son of W H Webber of Brighton he was educated at Brighton Grammar School and at St. John s College Cambridge He continued his medical studies at University College Hospital qualifying in 1912 On the outbreak of war in 1914 he joined the R.A.M C., in which he reached the rank of major While serving in Egypt he nearly died from a severe attack of typhus fever

After the war he held house-appointments at several London hospitals and he became resident medical officer first at the West London Hospital and later at University College Hospital In those days this appointment carried with it the task of administering the anæsthetics for emergencies and in this way Webber s interest was aroused in the subject which was to become his life s work. In the early 20s he was appointed assistant anæsthetist to the hospital and towards the end of the late war he reached the position of senior anæsthetist He also served on the staffs of St Paul s Hospital and the Royal Hospital for Diseases of the Chest

His published work included papers, with the late W H R Rivers, on the action of caffeine and alcohol on the capacity for muscular work He was co-editor, with the late F S Rood, of a textbook on *Anæsthesia and Anæsthetics* He held office as president of the anæsthetics section of the Royal Society of Medicine, and in 1948 he was elected a fellow of the Faculty of Anæsthetists of the Royal College of Surgeons He was also a senior fellow of the Association of Anæsthetists

C W M writes "Webber was a cheerful and reliable colleague, always ready to lend a hand in the working of the hospital, to whose welfare he was wholeheartedly devoted, and in whose service he never spared himself He could always be counted on to give a safe and skilful anæsthetic During the late war he was twice bombed out of his home, but he refused to quit London and throughout the blitz he continued to serve in the section of the hospital detailed to attend to casualties On his retirement from U C H he took over the duties of resident medical officer at St Luke's Hostel for Clergy, and up to the time of his last illness he gave them unstinted help To his colleagues he leaves a memory of a life-time of hard work, well and truly done"

Dr Webber married Madeleine Mary, daughter of Major J J Ryder, who survives him

## ROBERT STIVALA ASPINALL

C I E , F R C S E , Lieut. Colonel I M S retd

Lieut.-Colonel Aspinall died in a London hospital on Christmas day, at the age of 59 At the outbreak of the 1914-18 war, he was a medical student at Guy's Hospital He served for a time in the ranks, but later returned to his studies and qualified in 1916 He then took a commission in the R A M C , and he was wounded in action in 1917 while serving as a regimental medical officer in France In 1922 he joined the Indian Medical Service, and after only two years in the military division of that service he was selected for employment in the foreign and political department, where he spent the rest of his service

For some years he was the chief official practitioner at Delhi and Simla, the winter and summer capitals of India, and he was a notable success in both appointments In 1929 he became F R C S E , and in 1936, while still a major, he was appointed C I E During the greater part of the late war, as residency surgeon, Mysore State, he was stationed at Bangalore, the headquarters of the Southern Army The enormous increase in the civil and military population of Bangalore greatly added to the clinical and administrative work of this appointment, but Aspinall coped with it all with great skill Just before the transfer of power in 1947 he was selected for promotion to the post of inspector-general of civil hospitals in the Punjab

Shortly before his last illness he had remarried and settled in practice in the West End of London He leaves two sons by a former marriage

A colleague writes "Robbie Aspinall was well equipped by nature and study to deal with any professional or social emergency A clubbable man with a host of friends in London and all over India he will be much missed"

## ANDREW DEUCHARS

M B Glasg , D T M &H

Dr Andrew Deuchars, resident medical officer at Stonehouse Hospital, Lanarkshire, died on Oct 16 After graduating at the University of Glasgow in 1946, he was house-physician to the late Prof Noah Morris at Stobhill Hospital, Glasgow Later he served with the R A M C in Palestine, East Africa, and Mauritius In 1949 he became house-physician to Dr David Smith at the Royal Infirmary, Glasgow, and the following year he took his D T M & H. at Liverpool In the same year he was appointed junior hospital medical officer at Cleland Hospital, Lanarkshire, and soon afterwards took up his appointment at Stonehouse Hospital

T S C writes "When I first met Dr Deuchars, I was at once impressed by his attentive and thoughtful poise of mind It was in the clinical realm that I came to know his familiar presence so well and to feel the reinforcement of his able assistance He was one of those young men who did not fail to appreciate, from the ical standpoint, the full opportunities offered by overseas, especially in a tropical zone A keen ob he brought home much, to the enhancement of his acumen During the four years of his appoint Stonehouse Hospital the full promise of his men attainment became manifest The relief of the evening hour was a province which was part his own, and he was held in high esteem by all who had known his touch"

## Dr ELIZABETH CASSON

G de M R writes "The residential clinic Dr Casson founded at Dorset House, Bristol, patients who were only able to afford modest Later she extended her work by taking on the Pleasant nursing-home at Clevedon, Somerset, by the beginning of the war in 1939 she had 100 patients Owing to bombing, she moved the House clinic to Clevedon, using two more houses. she continued the principle of low fees and at admitted patients without charge She spent he herself, and she financed the Dorset House Sch Occupational Therapy in its beginning Indeed years passed before it was able to run at its level without financial help from her"

# Births, Marriages, and Deaths

## BIRTHS

MORRIS—On Dec 11, to Joan Ellen (née Bassett) wife of Morris, F R C S —twins (Caroline Melanie and Nicola bury)

WOLFF—On Dec. 15 at the Whittington Hospital, London, to Catherine wife of Dr Frederick Wolff—a son (Peter)

## MARRIAGES

MULCAHY—HANTON —On Dec 30 at the Church of the Im Conception Wexford Risteárd Mulcahy M D, M R C Aileen Hanton

# Appointments

ALDERS NICHOLAS M.D Vienna F R C.S M R.C O G consultant obstetrician and gynæcologist, Bournem East Dorset group of hospitals

BAINBRIDGE, CYRIL, O B E M.B Durh., D P H S A M.O., R H B Dundee

COPE D H P M B Lond F F A R C S consultant an Middlesex Hospital London

DAWSON MARJORY A , M B Glasg , D P H deputy M.O H.,

JONES, E D M B Lond D.M R T asst radiotherapist *Royal Marsden Hospital, London*

LEIPER JOHN M.B E M B Lpool D P H deputy coun West Riding of Yorkshire

MCLAUCHLAN, G P , M B Edin , D O H , D I H deputy and school M O , Exeter

REID J E , M B Belf , F F A R.C S , D A consultant an Belfast H M C

TAYLOR, JAMES O B E M B Glasg D P H , D T M & H area No 1 (Blaydon), M O H urban districts of Ryton and Whickham co Durham

WHITTLES, J H M.D , B.Sc Lond D P H deputy co and deputy principal school M O Trowbridge, Wilts,

WILSDON R B N , M D Lond M R C P consultant chest Middlesbrough tuberculosis administrative area

**North East Metropolitan Regional Hospital Board.**

EMERY, E W M B Brist F F R , D M R T consult therapist North Middlesex Hospital and annexes

MCKENDRICK G D W , M A B M Oxfd, M R C.P consultant physician in infectious diseases, St Ann Hospital

NAIRN C G , M B Glasg , F R C S E , M R C O G consultant obstetrician and gynæcologist, Prince and Bearsted Memorial hospitals

RUSSELL, ALEXANDER, O B E M D Durh M R C P D.P. part-time consultant physician in pædiatric end Queen Elizabeth Hospital for Children

TURK K A D , M D Lond whole time consulta logist Chelmsford group

**Birmingham Regional Hospital Board:**

CAPE R D T M D B Sc Edin M R.C P I whole t chest physician (S H M O ) Dudley and Stourbridge

GROVES J S M B Leeds F R C S D O M S part sultant ophthalmologist Coventry group

HARRINGTON J A M A Camb M.D Lond , D.P.H. D I H whole time consultant psychiatrist, Wh Hospital and Uffculme Early Treatment Hospital

SPRINGETT V H M D Lond. whole time consult physician, Birmingham (sanatoria) group and Bi *City Council*

YOUNG H B M B Glasg F R C.S.I F R F P.S., D.P. time consultant surgeon Wolverhampton group

# Notes and News

## OXFORD PLANS

the first half of their master plan for the development Radcliffe Infirmary site the board of governors of the d Oxford Hospitals on Dec 29 approved plans to provide accommodation for the Medical School of the University

board have agreed to provide 50 beds and laboratory accom tion on the Infirmary site for the Nuffield professor of medicine 50 beds and laboratories for the Nuffield professor of surgery ed and more suitable accommodation and workshops for the sor of anæsthetics; 25 beds and laboratories for a new regius sor of medicine who will be a clinician a new biochemistry tment considerable extensions to the pathology laboratories small extension for the department of radiology

e Ministry of Health have approved this whole plan in iple and the first part of it in detail, and are prepared to a financial contribution. The cost of these buildings no more than £400 000, and something over £200 000 will from university sources."

e second half of the master plan which has also been oved in principle by the Ministry of Health gives much d additional wards and departmental extensions. The rsity has agreed to give the same wholehearted support e rest of the plan (though it cannot give financial support) has given to the first instalment for the benefit of the cal school The board and the university are well satisfied these joint arrangements and are grateful to the Ministry alth for their interest and support

## ACCOMMODATION FOR HOSPITAL STAFF

Ministry of Health memorandum to hospital authorities[1] rks It has been represented to the Minister in the se of discussions he has had about the current shortage of r hospital medical staff that the provision of more resi ial accommodation by hospital authorities would con ite to the solution of this problem. The memorandum ves that the powers to provide residential accommoda conferred by the National Health Service Act are only ary to the main duty of providing hospital services; o these powers can appropriately be exercised only when essential to the proper conduct of the service Secondly not necessarily in the interests of the staff themselves they should live in accommodation provided by the al authority for hospital staff only Thirdly in view of tions on capital expenditure as little money as possible d be devoted to acquiring or building residential accom tion Accordingly hospital authorities should consider ling residential accommodation whether by purchase conversion new building or the allocation of existing modation only: (1) where the staff in question must o nature of their duties live on or near the hospital where the hospital is remote from any housing develop and no other suitable accommodation is obtainable in cality Where these criteria are satisfied married rs may also be provided for married staff Whether or hese two criteria are satisfied hospital authorities can aff to get houses, flats or rooms in other ways including proaches to local housing authorities and other land to obtain sympathetic consideration of requests by the question for rented accommodation and (*b*) maintain list of suitable flats &c for the information of those eed accommodation

## SOME SHELTERED WORKSHOPS

Newhaven on the hill once justly no doubt called Pleasant (but now covered with steep haphazard little streets) is Searchlight a sheltered workshop for verely handicapped which has lately come of age[2] light takes its name from an old Army searchlight set up to defend us against the Zeppelins of the 1914-18 It owes its rebirth to an enterprising member of the g profession Miss Muriel Powell who is still at its head Powell had been matron at the marine branch of the g Craft School at Tidemills and had seen the cheerful d children pass out of her care to become—once the ment of their homecoming was past—a burden on their s, or inmates of chronic wards She decided if she to change that; and in 1933 with three pioneer d boys she walked into the small bungalow she had to launch her venture She found three things waiting for her a telegram of good wishes, a letter advising her not to put all her eggs into one basket and a steak and kidney pudding It was the letter that went into the basket—the waste-paper basket The other offerings, too were dealt with appropriately Since that day the bungalow has developed into a group of large and well-equipped workshops flanked by dormitories recreation rooms cottages for staff kitchens and a big dining hall which was added only last year The three pioneers were the forerunners of 44 men so severely handicapped that they are not employable in ordinary industry and hence do not qualify for the disabled persons register

In the early days Searchlight men made sweets and jam but just as a flourishing business was being built up along came the 1939-45 war to kill it stone dead with rationing Fortunately some new lines of work—wooden toy making carpentry and boot-repairing—were already being tried and presently weaving leather work and soft toy making were added The labour of running the place in war time was particularly arduous At one time Miss Powell as the only able bodied person in the place had to lift the more helpless men out of their beds into Morrison shelters when the sirens went at night and back again at the all clear With the return of peace she extended the work and had the good fortune to gather some keen and capable staff about her

There had been financial struggles from the start When her own capital ran out she was able to get local authorities to pay £1 a week maintenance grant for each man; and when this proved too little she started a farthing fund There have also been donations from friends, funds collected at a Searchlight week in Newhaven and raised by special efforts and—in recent years—donations from large voluntary funds and some commercial firms. The aim has always been to make Searchlight ultimately self supporting but the overhead costs of such a venture are high and in the meantime it needs the full support of its friends

Not long ago the Central Council for the Care of Cripples published a survey[3] of sheltered workshops and home industries run by their member organisations in south east England Besides Searchlight the workshops include Cripplecraft at Herne in Kent Hostels for Crippled and Invalid Women in south-east London Queen Elizabeth's Training College for the Disabled at Leatherhead the School of Stitchery and Lace at Bookham Grange the Woodlarks Workshop at Farnham and the Yately Textile Printers in Hampshire At Cripplecraft which is not a training centre but mainly occupational the work done includes soft-toy making basketry chair caning and woodwork; Queen Elizabeth's Workshop specialises in floral pottery and Yately in block printing of textiles by hand Bookham Grange and the Hostels for Crippled Women do fine needlework embroidery and some dressmaking and Woodlarks produces wooden toys There are home industry schemes at Brighton Hove Chichester Croydon and Kingston-on-Thames which in July 1953 (when the survey was made) were providing work for 575 men and women The work includes glove and slipper making knitting soft toy making weaving netting embroidery basket work chair caning woodwork and a number of other crafts.

Miss Norah Hill who made the survey comments that new legislation has led to an increasing awareness of the needs of the physically handicapped without so far the development of any increased provision to meet these needs There has however been a great growth of friendly feeling she finds, between Government departments local authorities and voluntary associations. The local authorities have recognised that most voluntary bodies working for the disabled "far from being inefficient, do the same job at less cost because they are able to keep down the overheads" As a result nearly all local authorities have now increased their grants to the voluntary bodies on whom they depend for services The prospects of setting up more residential sheltered workshops are poor at present but she thinks it might be possible to experiment further with non residential work centres for small groups

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### Eli Lilly Medical Research Fellowship

Applications are invited before April 15 from doctors registered in South Africa for this fellowship (250 dollars a month) for study in the United States Further details can be had from Dr H A Shapiro P O Box 7015 Johannesburg

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(54)115

Story of Searchlight Searchlight Cripples Workshops unt Pleasant Newhaven Sussex 1954 Pp 33 2s 6d

[3] Some Notes on Sheltered Workshops and Home Industries for the Seriously Disabled in Southern England Central Council for the Care of Cripples 34 Eccleston Square London S W 1 Pp 31 3d

## University of Cambridge

The following degrees were recently conferred

*M D*—J J Fleminger

*B Chir*—Inez R Aldous William Atherton, D W Atkinson I H Backhouse J W Blaxhill L H Blonstein, J N Bodger W R. P Bourne P J Burrows J R Burwell S T G Butterworth P G T Bye D H Cameron T R Clendon, W L Cordeaux P D Crockatt J A Dryden John Fairley I McL Flowers J S Garfield, E F D Gawne, R H S Gibbs J N Godlee Claudia M. B Grigson, L H Hurrell, R D Hyde A C Johansson P J D Kirk A H Labrun I V Longfield J S Miller, R C Rainby Luxmore W S Ogden, D B R. Osbourne, A M Parfitt R I C Pearson, D J H Prosser, Edward Redfearn, C F Ridley I R Robertson M S Robson Ian Ross Russell C E Salter Rudolph Schram, G C Spackman, G F W Swan, M J Turner, J F Walker

*M B*—S G Bayliss G F B-Birdwood D J Buttery, W H Catling John Crook R. H Gibbon J T Gibbs, J W Harding G H Hilton Harold Jacobs R. J Knight R C Lawson, S P Lock, C M. McGregor, H C Masheter Lucy M Rochelle, J K Snell I G Tait D E Tunnadine, P D W Wickenden W A Williamson, J R Wood

## University of London

The title of professor of zoology has been conferred on Mr G P Wells, SC D, in respect of his post at University College, London

On Dec 15 the degree of M D was awarded to P J Hare

## University of Glasgow

The University, with the Western Regional Hospital Board, has appointed Dr A C Forrester to the senior lectureship in anæsthetics which has been set up within the St Mungo department of surgery at Glasgow University and Glasgow Royal Infirmary The appointment carries the clinical ranking of consultant

Dr Forrester is chairman of the anæsthetic services subcommittee of the Central Consultants and Specialists Committee (Scotland) He is a consultant anæsthetist at Glasgow Royal Infirmary with which he has been associated for the past 18 years During that time he has shared in the teaching of anæsthetics to students and post graduates Dr Forrester has interested himself in the early introduction of curare into anæsthesia, and circulatory changes during anæsthesia. He has visited many other departments of anæsthesia in this country and abroad, spending some time in the U S A and Canada

Dr R C O Saunders has been appointed assistant to the senior lecturer in anæsthetics

## Royal College of Surgeons of England

Normally admission to the Hunterian festival dinner is by invitation, but this year it will be held for the first time in the new great hall of the college, and it will be possible to admit, on payment, up to 100 fellows and members Those who wish to attend the dinner, which is to be held on Feb 14, should write immediately to Mr W F Davis, deputy secretary of the college, Lincoln's Inn Fields, London W C 2, enclosing a cheque for £2 15s to cover the inclusive cost of the dinner

## International College of Surgeons

The college offers a fellowship of $3000 to a young graduate in medicine from a European or South American country

The scholarship is for travelling expenses and maintenance for twelve months Before it can be confirmed candidates must secure an appointment as a resident or fellow for one year of study and graduate work in one of the teaching centres in the United States or Canada Further particulars may be had from Dr J F Brailsford, 20, Highfield Road, Edgbaston Birmingham 15

## Royal Society of Medicine

The W J Harrison prize in laryngology has been awarded to Mr C P Wilson, and in otology to Miss M R Dix The Norman Gamble prize has been awarded to Mr J C Seymour and a Norman Gamble research grant of £100 has been made to the Institute of Laryngology and Otology

The next award of the William Gibson research scholarship for medical women (£200 p.a) will be made in July 1955 Further particulars may be had from the secretary of the society, 1 Wimpole Street, London, W 1

## Nuffield Dental Fellowships

One of the aims of these fellowships is to enable graduates in medicine and science to qualify themselves to undertake teaching and research on dental health and disease Further particulars will be found in our advertisement columns

## Royal Statistical Society

*Study Circle on Medical Statistics*—On Wednesday, Jan 12, at 6 P M at the E L M A Lighting Service Bureau, 2, Savoy London W C 2, Mr R H Thouless, SC D, will deliver on Statistics in Parapsychology

## Not Enough Nurses

Owing to shortage of nurses (says the *Richmond & T ham Times* of Dec 18) 47 beds have been closed Normanfield Mental Hospital, Teddington Because on the staff only medium grade and high grade pat be admitted in future For some time past only children have been admitted and many of these have a heavy burden on the staff The Hon John F the chairman of the North West Metropolitan Hospital Board, said that the staff situation at oth and mental deficiency hospitals was also critical Italian nurses, he added, had been recruited for two

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CORRIGENDUM *The Design of Clinical Experim* lecture by Dr D D Reid, which was one of a series on the Basis of Medicine, delivered by various speakers at the of the British Postgraduate Medical Federation was give London School of Hygiene and Tropical Medicine—not, in a footnote (Dec 25 p 1293) at the Postgraduate Medical of London

*Archivos de Neurobiologia*—This Spanish journal for psychiatry, and child psychiatry which was founded in Ramon y Cajal and ceased publication during the civil been started again. Dr B Llopis, director of the neurop hospital in Madrid, is editor in-chief and Dr F Pollak downe Road, Hove 2, is on the editorial board

The address of the British Tuberculosis Association 59 Portland Place, London W 1 (tel Museum 3810)

# Diary of the Week

JAN 9 TO 15

### Tuesday, 11th

ROYAL COLLEGE OF PHYSICIANS OF LONDON Pall Mall East
5 P M Dr G B Dowling Scleroderma and Dermatomy (Watson Smith lecture)

ROYAL COLLEGE OF SURGEONS OF ENGLAND Lincoln's Inn W C 2
3 45 P M Dr Joseph Bamforth Early Beginnings of Ca (Imperial Cancer Research Fund lecture)

ROYAL SOCIETY OF MEDICINE, 1 Wimpole Street W 1
8 P M *Psychiatry and Neurology* Prof Alfred Meyer Te lobe Epilepsy and the Hippocampal Region. Dr Whitty Cingulectomy Dr H Hassler (Freiburg) Method of Stereotactic Brain Surgery (Film dem tion)

ST MARY'S HOSPITAL MEDICAL SCHOOL Paddington, W 2
5 P M Dr P L Mollison The Rhesus Factor

INSTITUTE OF DERMATOLOGY St John's Hospital, Lisle W C 2
5 30 P M Dr R G Cochrane Leprosy

CHELSEA CLINICAL SOCIETY
8 30 P.M (Rembrandt Hotel Thurloe Place, S W 7) Petrie Mr E D O Brien Problems of Modern Di

MANCHESTER MEDICAL SOCIETY
8 P.M (Medical School, Manchester) *Surgery* Mr D W Calcinosis Circumscripta Mr J K Wright Replacement of Bone

### Wednesday, 12th

ROYAL SOCIETY OF MEDICINE
4 30 P.M *Physical Medicine* Dr Hugh Burt Dr Donald Dr C E Quin Hydrocortisone

MIDLAND MEDICAL SOCIETY
8 15 P.M (Birmingham Medical Institute 154 Great Street Birmingham, 3) Dr Robert Forbes Developments in Medical Litigation

MANCHESTER MEDICAL SOCIETY
4 30 P.M *Medicine and Pathology* Prof C H Gray Studies of Urinary Adrenal Steroids

### Thursday, 13th

ROYAL COLLEGE OF SURGEONS OF ENGLAND
5 P.M Mr C P Wilson Lateral Cysts and Fistula of Developmental Origin (Hunterian lecture)

ALFRED ADLER MEDICAL SOCIETY
8 P M (11 Chandos Street, W 1) Dr A A Mason Hypnosis in Skin Disorders

NUFFIELD ORTHOPÆDIC CENTRE, Wingfield Morris Hospital, Oxford
8 30 P M Major L C Hollister Jun Internal Fractures

LIVERPOOL MEDICAL INSTITUTION 114 Mount Pleasant Liv
8 P M Dr Robert Kemp Dr I Harvey Flack Medical of Patient and Public

UNIVERSITY OF ST ANDREWS Medical School Small Dundee
5 P M Dr T Cecil Gray Anæsthesia in the Age of Stre

### Friday, 14th

INSTITUTE OF DERMATOLOGY
5 30 P.M Dr Cochrane Leprosy

ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GL 242 St Vincent Street Glasgow
5 P M Mr Arthur Jacobs Surgical Approach Pathology of the Kidney

### Saturday, 15th

BIOCHEMICAL SOCIETY King's College, Strand, W C 2
2 P.M Scientific Papers

# ANÆSTHETIST LOOKS AT A BURNT CHILD

D W SHANNON

M.B Edin F.F.A R C.S

SULTANT ANÆSTHETIST ROYAL HOSPITAL FOR SICK CHILDREN EDINBURGH

> e success of surgical treatment depends on the sum of a host ispensible contributions The best results follow only each member of a hospital team, doctors and nurses alike out their allotted task punctually and perfectly" (Learmonth

the treatment of few surgical conditions is this truth r demonstrated than in the care of a seriously burnt The prevention and the treatment of shock the ration of burnt surfaces for grafting, the outcome ese operations the relief of pain from dressing and maintenance of metabolic requirements depend not chniques of a single individual but on the coördinated s of all members of a surgical team and the ability ich member to appreciate the problems of his agues.

e purpose of this paper is to review the position of næsthetist in such a team to indicate his approach o challenge, and to suggest possible approaches to the problems as they arise

## revention and Treatment of Oligæmic Shock

matter what is the cause of oligæmic shock, its iate effect is anoxia Recent work has shown that o anoxia converts shock from a reversible process n irreversible state

oxia is also the most common cause of anæsthetic lications. Awareness of its likelihood and its nition and early treatment, are fundamental to anæsthesia It follows therefore, that the anæs st is well equipped by training and experience to o on the treatment of shock following burns

addition to correction of the ætiological factor the ment of shock should be aimed at easing the burden ie vital systems by increasing the available oxygen y by improving its transport to the tissues, and ducing the demand by the tissues

### OXYGEN TRANSPORT

er a burn fluid is lost and red cells are destroyed oportion to the extent and depth of the burn losses initiate shock and correction by replace of blood and fluid is urgent and imperative.

ere is a tendency to disparage the giving of whole and to favour the replacement of lost fluids with ia and plasma expanders alone yet in an extensive the resulting massive destruction of red cells and of hæmoglobin reduce the total oxygen capacity circulating blood to dangerous levels and present mmediate grave prognosis particularly in the The hæmoglobin lost can be made good only by fusion of whole blood The use of whole blood ver should not be confined to the extensive burn burnt patient with healing delayed beyond three has *depressed marrow function with a low red* cell count If this secondary anæmia is allowed to persist a metabolic disturbance is set up which has serious consequences to the patient It must be treated by repeated blood transfusions which aim at maintaining a hæmoglobin level of 80%

All patients with burns of more than 10% of their surface area require intravenous therapy to counter shock The volume of fluid given must be carefully calculated if it is to be adequate and overloading of the circulation is to be avoided

Empirical assessment can never be satisfactory even in expert hands Various formulæ are available That introduced by Barclay and Wallace (1954) combines safety with effectiveness and simplicity Their formula is based on the extent of the burn (fig 1) in relation to the patient's age (table I) and specifies the number of millilitres of plasma and electrolyte per 1% of body-surface burnt The calculated total is divided into three equal parts a third being given in the 8 hours immediately following the injury a third 8–24 hours after and the remaining third 24–48 hours after

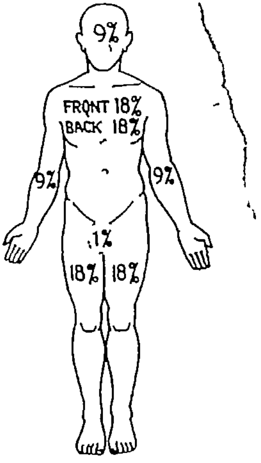

Fig 1—"Rules of nine" for estimating area of burn

Consider for instance a child aged 18 months admitted 2 hours after injury with burns involving 20% of his body-surface According to table I the requirement is 15 ml of plasma and 15 ml of saline solution for each 1% of body surface burnt Therefore 48 hours requirement for this child is 15 × 20 = 300 ml. of plasma + 300 ml of saline solution. *His requirement for the 8 hours immediately* following the burn is 100 ml + 100 ml. and this quantity must be given in the first 6 hours of treatment because he was admitted 2 hours after injury

Table I applies to burns of up to 30% of body-surface. For more extensive burns estimations from this table would lead to overloading of the circulation and volumes equivalent to 10% body weight should be given (table II)

It is important to remember that these amounts of fluid replace only the fluid lost as a result of the burn and are therefore termed replacement fluids A further adequate volume must be given to cover the normal metabolic fluid requirements of every child (table III) Such volumes are termed requirement fluids.

Replacement fluid for patients with burns of less than 10% of the body surface is given by mouth and for patients with burns of more than 10% of the body *surface intravenously*

I—BURNS OF UP TO 30% OF BODY-SURFACE : PLASMA AND ELECTROLYTE REQUIREMENTS IN FIRST FORTY EIGHT HOURS AT DIFFERENT AGES

| luid | Age (yr) | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Birth | [illegible] | [illegible] | ¾–1 | 1–2 | [illegible]–3 | 3–4 | 4–5 | [illegible]–6 | [illegible]–7 | 7–8 | 8–9 | 9–10 | 10–11 | 11–12 | [illegible]–13 | 13–14 | 14–15 | [illegible]–16 | 16–[illegible] | 17–[illegible] | Adult |
| lyte n (ml) | 7 | 10 | [illegible] | 13 | 15 | 21 | 24 | 27 | 31 | 35 | 40 | 44 | 46 | 51 | 56 | [illegible] | 67 | 78 | 88 | 96 | 104 | 110 |
| s (ml) | | 10 | 12 | 13 | 15 | [illegible] | [illegible] | [illegible] | 31 | 35 | 40 | 44 | 46 | 51 | 56 | [illegible] | 67 | 78 | 88 | 96 | 104 | 110 |

Per 1% of body-surface burnt

TABLE II—BURNS OF OVER 30% OF BODY-SURFACE AVERAGE WEIGHT AT DIFFERENT AGES, FROM WHICH REQUIREMENT IN FIRST FORTY-EIGHT HOURS IS CALCULATED

| — | Age (yr) | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Birth–3/12 | 3/12–6/12 | 6/12–9/12 | 9/12–1 | 1–2 | 2–3 | 3–4 | 4–5 | 5–6 | 6–7 | 7–8 | 8–9 | 9–10 | 10–11 | 11–12 | 12–13 | 13–14 | 14–15 | 15–16 | 16–17 | 1 |
| Weight (kg) | 5 | 7 | 9 | 10 | 13 | 15 | 17 | 18 | 20 | 22 | 24 | 26 | 29 | 32 | 35 | 39 | 43 | 48 | 54 | 59 | 65 |

For each kg 100 ml of fluid should be given

TABLE III—FLUID INTAKE (AS GLUCOSE DRINKS OR WATER) REQUIRED TO COVER NORMAL DAILY ME REQUIREMENTS

| — | Age (yr) | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Birth–3/12 | 3/12–6/12 | 6/12–9/12 | 9/12–1 | 1–2 | 2–3 | 3–4 | 4–5 | 5–6 | 6–7 | 7–8 | 8–9 | 9–10 | 10–11 | 11–12 | 12–13 | 13–14 | 14–15 | 15–16 | 16–1 | 1 |
| Metabolic requirement (ml) | 700 | 1000 | 1150 | 1200 | 1300 | 1400 | 1400 | 1400 | 1500 | 1500 | 1500 | 1600 | 1600 | 1700 | 1700 | 1800 | 2000 | 2200 | 2400 | 2600 | 2 |

As already indicated, the restoration of circulating blood volume is of little value if its oxygen-carrying capacity (hæmoglobin) remains deficient In all patients with deep burns, and in all patients with extensive superficial burns involving more than 25% of the body-surface, where the destruction of red cells has been considerable, half the total intravenous replacement fluid should be given as whole *fresh* blood, the other half being given as equal parts of saline solution and plasma

In addition to replacement fluids, metabolic requirement fluids are given by mouth hourly unless the patient cannot retain oral fluid, as in gastric stasis and burns of the mouth, when it is also given intravenously as 5% dextrose in water

### OXYGEN SUPPLY

The urgent need for fluid replacement must not blind the clinician to the fact that anoxia, although initiated in burn cases by a decrease in the oxygen carrying capacity of the blood, is maintained and indeed exaggerated by other factors which, although not serious in themselves, may either in association with blood-loss or through their cumulative effect jeopardise the patient's recovery

Clinical anoxia cannot be classified into the compact compartments defined by Barcroft Oxygenation of the tissues depends on the integrity of several interdependent systems (fig 2), impairment of any one of which must necessarily affect all Each system must be carefully checked, if irreversible damage from anoxia is to be prevented The lungs are the reservoir from which the blood draws its oxygen In the period immediately following a burn, when blood and fluid are to be replaced, it is important—perhaps vital—that the tension and volume of oxygen in the lungs be maintained at optimal levels This depends on a clear airway and minute pulmonary ventilation

#### *Airway*

This can readily become obstructed The breathing of hot irritating fumes may cause laryngeal œdema or lead to the accumulation of desquamated cells and mucopurulent secretions in the tracheobronchial tree The patient will be cyanosed and will struggle for breath The need for clearing the airway is imperative, and treatment by tracheotomy or by bronchoscopic aspiration will, where necessary, take precedence over the replacement of fluids

Less dramatic causes of respiratory embarrassment may tend to pass unnoticed, but their very persistence in a shocked patient can delay recovery and may on occasion eventually endanger life Crusting of secretions ithin the nasal vestibules is common not only in burns olving the face but also in any dehydrated child orces mouth breathing with all its harmful effects Thick viscid postnasal secretions ooze down in laryngeal region and cause exhaustive bouts of and intensify respiratory embarrassment Some *ago a child in this unit died from asphyxiation* mucous crust blocking the laryngeal aperture cause of this sudden unexpected death was not ciated until necropsy Without doubt the nurse give the same scrupulous attention to oral and hygiene as to the care of the burnt surface

Other simple happenings, innocent in themselve often overlooked Lolling of the child's head pillow may lead to obstruction of the airway, if the tonsils and adenoids are enlarged In child, if the airway cannot be maintained by procedures, a nasopharyngeal airway lubricated analgesic (2% cinchocaine) ointment should be pass

Again, if the circulation is overloaded by replacement of fluids, a transudate fills the spaces and interferes with the diffusion of oxyge the alveolar capillary membrane This danger by the primitive and uncertain method (external on rubber tubing) by which the flow of fluids patient is apt to be encouraged It is a complicat readily occurs in young children with their small

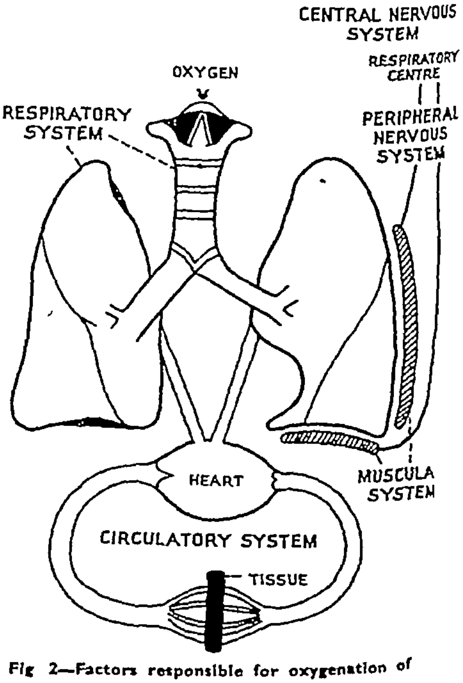

Fig 2—Factors responsible for oxygenation of

blood volume. The compromise between too little too much can be achieved only by careful and con d supervision of the drip Too often this super n is left to the nurses who lack the experience and knowledge which the safety of the child demands, furthermore it is not their responsibility

*ute Pulmonary Ventilation*

ie tension and the volume of oxygen in the lungs nd on the summation of the rate and depth of thing This depends on the integrity of the respira centre and the efficiency of the respiratory muscles r a burn there is central stimulation due to pain and *The rate of breathing is increased without a propor* ate increase in the depth This rapid shallow breath is particularly common in children with burns lving the chest and abdomen. By the relative increase ie dead air volume and the speed at which air is being n through the narrow tracheobronchial tree this type reathing is inefficient obstructive and exhausting to child The child must be given relief through the *ful administration of opiates.* Further precautions t be taken to ensure that the harmful effects are not ggerated by the application of heavy blankets or stricting bandages, and that the high Trendelenburg tion does not interfere with free intercostal and hragmatic movements

pinions differ about the value of oxygen in the tment of shock. The claims for oxygen therapy how can never be dismissed lightly since time and again he course of one s duties its undoubted value has been erienced In this unit oxygen is given routinely to dren with burns involving more than 30% of the body ace, and to any child in whom there is evidence of a ction in the pulmonary ventilation and of peripheral ulatory failure High concentrations of oxygen ease the volume and tension of oxygen in the pulmon alveoli and used as a therapeutic adjuvant, tide the nt over a period of acute anoxia while efforts are made to correct the deficiency in the circulating l volume Its value depends on a clear airway gen can neither correct nor surmount an obstructive er) and the care with which the apparatus is con d and maintained Too often one sees the oxygen der with its connections carelessly fitted fizzing uselessly or the thin rubber tubing conducting en to the patient may be kinked as it leaves the der and arches over the bed head; or a perished piece with harness inaccurately adjusted is sed and twisted and obstructs the patient s airway t of all the humidifier may be incorrectly fitted water will be siphoned into the lungs.

ygen is best given to children through an intra- catheter with several holes in its terminal inch to rse the gas and to prevent the gas from impinging antly against one spot The tube should be ated with analgesic ointment and strapped over nasal bridge and forehead leaving sufficient slack ow free movement of the child s head

ygen is delivered through a humidifier at a flow f 2–3 litres a minute and once every 12 hours the must be removed and replaced through the alternate l

y if attention is given to every detail can one be n that oxygen is being given as a therapeutic ure and not as a therapeutic gesture.

### OXYGEN DEMAND

he post war years have taught anything it is that goods are scarce one must economise in their u e simple economic law might be applied with advan o the treatment of shock In this state as has been ted, interference with the transport of oxygen ts its supply to the tissues, and the demands of the s must be reduced accordingly Consideration must be given to the handling of the patient and to the control of anxiety restlessness

TABLE IV—DOSAGE TABLE OF PREOPERATIVE AND POST-OPERATIVE DRUGS

| Age (yr) | Weight (kg) | Quinal barbitone sodium (gr) | Atropine (gr) | Diamorphine hydro-chloride (gr) |
|---|---|---|---|---|
| Birth–1 | 10 | — | 1/[illegible] | 1/[illegible] |
| 1–2 | 13 | [illegible]/4 | 1/[illegible] | 1/[illegible] |
| 2–3 | 15 | [illegible]/4 | 1/[illegible] | 1/[illegible] |
| 3–6 | 20 | 1 1/4 | 1/[illegible] | 1/[illegible] |
| 6–9 | 26 | 2 1/4 | 1/100 | 1/[illegible] |

*Handling of the Patient*

This must be reduced to a minimum only essential diagnostic and therapeutic measures being permitted. These measures must be taken with speed and precision by doctors and nurses versed in their intricacies Skill and experience are required in feeding and in setting up blood transfusion apparatus for a young child These important measures cannot be left to an inexperienced nurse or houseman who may labour for an hour or more exhausting the child and themselves before calling for assistance

*Anxiety and Restlessness*

These must be relieved Care must be taken however before administering depressant drugs that restlessness is an evidence of pain and not visible evidence of the patient s fight to relieve tissue anoxia.

Sedative drugs must be used circumspectly and their effect on the rate and depth of breathing must be carefully observed Diamorphine hydrochloride is our drug of choice for children and is given, on admission in doses based on the age (table IV) half the dose being given subcutaneously and half intravenously The dose may be repeated 4 hourly

Diamorphine hydrochloride may seem an unusual drug to select It has been used routinely in this hospital for many years as a postoperative sedative and it was a natural choice in burnt children The reputed respiratory depressant effect of diamorphine hydrochloride however with the threat of anoxia encouraged investigation of the potentialities of morphine and the barbiturates. Neither gave satisfaction. Idiosyncrasy to morphine is not uncommon in children making it unsuitable for routine use and its respiratory depressant effect appeared more pronounced than that of diamorphine hydrochloride The barbiturates (quinal barbitone sodium and phenobarbitone) as might be expected excited rather than depressed the child in pain and their repeated administration exerted a cumulative effect with prolonged and undesirable drowsiness.

On occasion a seriously burnt child has received an overdose of opiate before admission An infant aged 3 weeks admitted to this unit had been given gr 1/8 of morphine The pulmonary ventilation volume, in such a case may be reduced to a dangerous level, and it may be necessary to assist the child s breathing Oxygen is given through an *endotracheal tube, if necessary by* rhythmic manual compression of the rebreathing bag of an anæsthetic machine until the patient can actively maintain adequate ventilation

### Pre-anæsthetic Assessment

The general disturbances effecting and resulting from oligæmic shock having been corrected and brought under control consideration must next be given to the local treatment of the burn *This treatment varies from* the application of a simple dressing to extensive cleansing and grafting It therefore becomes necessary to assess the capacity of the patient to meet these operations If this assessment is to be made with any degree of accuracy the anæsthetist must be aware of the following factors

(1) The clinical state of the patient

(2) The nature of the operation, its benefits to the patient, and the metabolic and physiological disturbances associated with it

(3) The hazards of the particular anæsthetic technique required to provide satisfactory operating conditions for the surgeon

(4) The capability or possibly more important, the limitations of the surgeon and the anæsthetist

Just as the preparation of a burnt child is directed towards easing the burden on the respiratory and cardiovascular systems, so the assessment of the burnt child depends on the functional efficiency of these systems This assessment can be made only on clinical grounds Special investigations and reports by non clinical departments, although informative in a later review of the case, are necessarily delayed and often confusing, and their importance tends to be overemphasised The seriously burnt patient cannot be assessed from a single clinical examination, since the response of a shocked child, and the manner of his response, to restorative measures and replacement therapy can vary from hour to hour The clinician should rely on frequent bedside observations the colour of the skin and mucosæ, the temperature of the skin, the feel of the pulse, the capillary-filling time, the rate and rhythm of breathing, and the dryness of the tongue and lips—attempting by experience to acquire something of the clinical perception of the physicians of yesteryear

The clinician anæsthetist accompanies the surgeon on his repeated visits from the time of the child's admission to hospital, and from observations must be prepared to discuss, at any time, the advantages or dangers to the patient of whatever operation the surgeon may consider advisable

The early local treatment of burns—cleansing and the application of dressings—presents few problems to the anæsthetist The immediate threat of shock has been relieved, and these operations can be done under diamorphine hydrochloride, or the patient can be given low concentrations of cyclopropane, the gas being used as a form of controlled sedation

Later, usually between the 10th and 14th days after a burn, sloughs begin to separate, and a decision must be made about the best time for excising the eschar, whether extensive excision and grafting of the raw surfaces should be done, or whether the burnt area should be treated piecemeal

After extensive deep burns the patient's condition may begin to deteriorate between the 7th and 10th days The child becomes fevered and chesty, with a rapid pulse, or, as has happened in three cases in this unit, becomes hypopyrexial, disoriented, and later comatose It is just such patients, however, who benefit most from heroic, rather than conservative, measures The anæsthetist must be sufficiently informed on the benefits of this action to advise the surgeon on the child's ability to stand the stress of extensive surgery, and whether the anticipated blood loss can be replaced by immediate blood-transfusion or prevented by using a hypotensive drug

The custom of referring seriously ill patients to physicians for preoperative assessment is to be deplored Any member of a surgical team should be better equipped to advise than a physician, who is ill-informed on many of the essential physiopathological upsets The custom is less common than it was, but physicians, from time to time, with an enviable disregard for the hazards of anæsthesia, record as their considered opinion that a seriously burnt child will survive an operation of uncertain nature, providing a non-toxic agent, such as nitrous oxide, is used

I submit that the anæsthetist to the surgical team is [illegible]t equipped to advise on the resultant of the four [illegible]bles mentioned above He is familiar with the [illegible]ls of anæsthesia His training has taught him to appreciate the effects on the patient of blood surgical trauma associated with particular He knows, none better, the capabilities of his

### Pre-anæsthetic Medication

Atropine is given to all patients in a dose prop to the age of the patient Children tolerate large amounts of atropine and rarely show uncomfortable looking buccal and labial characteristic of the atropinised adult

In the weeks immediately following a seve repeated anæsthetics are necessary to permit and grafting operations During this period basal metabolic rate rises rapidly and may raised for several months This necessitates a intake well above normal requirements, and fr 2nd day onwards it is the custom, in this unit, for to be put on a carefully planned diet Recove anæsthesia must be rapid and uncomplicated ference with this dietetic régime is to be avoid anæsthetist should aim at having the child aw minutes of completion of the dressing or oper that food may be given within an hour or tw leaving the operating theatre For this re operative sedation is rarely used This is expressed opinion of psychiatrists, but exp given little support to their anxious forebodings or possibly because of, repeated anæsthetic the child is surprisingly coöperative, appears the frequent visits to the theatre, and, with th thetic technique detailed below, goes to sleep quietly

The occasional child who refused to become reconciled to visiting the theatre is barbitone sodium by mouth (for dosage see table drug usually puts the patient to sleep and, the rate at which it is metabolised, recovery effects is fairly rapid

Should an operation be necessary in the period diately following a burn, the child is controll diamorphine hydrochloride At this time requirements are satisfied by parenteral

The hæmoglobin level must be estimated preoper and any anæmia corrected For grafting op during which the removal of skin and the granulations will cause blood loss, it is essential blood-transfusion should be given in the preoperative period and again during the to replace any loss

### Anæsthetic Technique

Once upon a time an inspired surgeon attributed the unfortunate death of one of hi to his (the patient's) failure to " stand the an Since then this aphorism has been to the surg enlargement of the thymus has been to the an and a surgeon, before subjecting a seriously i to a lengthy and hazardous surgical operation heard to ask the anæsthetist to examine th and report on his fitness to " stand the anæsth

A review of the literature on anæsthesia, would almost certainly show that it is not the ill patient who is likely to die from an anæs the robust healthy child who has been badly Further investigation would show that the could invariably be attributed to some avoids cretion on the part of the anæsthetist The se patient appears to be unusually resistant to of anæsthesia and occasionally appears to be condition after the operation than he was before

This paradox is explained by the fact that the ill are normally anæsthetised by experienced an They are less resistant to the effects of and satisfactory operating conditions may

maintained with relatively small amounts of anæs
s In addition modern anæsthetic techniques
om being a danger to the patient embrace the
als of resuscitative therapy rest, positioning
n blood transfusions, &c
ler anæsthesia the patient is at complete rest ;
irway is carefully maintained oxygen is given in
concentration and with positive pressure if necessary
and depth of breathing are maintained at optimal
; the pulse colour, and blood pressure are con
ly observed and their significance interpreted
is given where necessary to replace loss during
sive grafting operations and the rate of the trans
is regulated to satisfy the immediate needs of
atient

s seriously burnt child to whom these restorative
res are so vitally important, shows benefit from this
ntrated attention and, providing the surgical opera
s completed without unnecessary surgical trauma
rs in better clinical condition after the operation

*hetic Agent*

's impossible to dogmatise on the best anæsthetic
for a burnt child Indeed the flood of literature
ting from different centres and extolling the
s of particular drugs for similar operations must
y confusing to the casual anæsthetist and neutral
er The truth is that the patient's safety does not
l on the pharmacology of an anæsthetic drug so
as on the skill and experience of the anæsthetist
istering it, combined with careful preparation and
ticulous application of whatever anæsthetic
que is decided on

sthetic drugs are used essentially to provide
tory operating conditions which, in similar
ons vary with individual surgeons One may be
work competently with a lightly anæsthetised
where another would require and demand
rarised pulseless, apnœic anthropomorphous
opularised by the modern anæsthetist

unately, in burns the requirements of the surgeon
All he asks is a quiet patient and access to the
areas. It is possible therefore for the anæsthetist
centrate on the demands of the child These are
ows :

rapid smooth induction free from coughing struggling
ying which exhaust the child and stimulate the
on of obstructive secretions.

high concentration of oxygen to satisfy the thera
nd increased metabolic demands of the burnt child

uiet breathing

inimal disturbance of metabolic and physiological
s The surgical team has already spent many hours
ing to correct the upset caused by the burn

apid recovery to allow full and early expansion of the
nd rapid resumption of the dietetic régime

propane is well suited to meet these demands of
l It may be given with high concentrations of
and being excreted unchanged produces minimal
f the body chemistry Its central depressant
nsures quiet breathing but most important is
a gas Absorbed and expelled through the lungs
the anæsthetist to control not only its adminis
but also its excretion This combined with the
t cyclopropane is a powerful non irritant agent
of taking a child from consciousness to respira
st in 60–75 seconds makes it the most flexible
trollable of agents, permitting rapid smooth
easy maintenance and return to consciousness
aving the operating table Feeding may be
2 3 hours later

*Administration*

ropane is administered with circle absorption
o very young (aged less than 3 years) with a
orption

TABLE V—ENDOTRACHEAL TUBES : DIMENSIONS OF MAGILL ORAL TUBES

| Dimension | Age (yr ) | | | | | | |
|---|---|---|---|---|---|---|---|
| | 3/12 | 9/12 | 1½ | 3 | 5 | 9 | 12 |
| Size no<br>Length (cm ) | 00<br>10–11 | 0<br>11–12 | 1<br>12–13 | 2<br>13–14 | 3<br>15–16 | 4<br>17–18 | 5<br>18–19 |
| Ext diam. (mm ) | 4·3 | 5·6 | 6·0 | 6·6 | 7·6 | 8·3 | 9·0 |

Rapid induction to surgical anæsthesia is achieved after five or six breaths (30–40 seconds) by giving high concentrations of cyclopropane the proportion of cyclopropane to oxygen being 3 to 1, and anæsthesia is maintained with a flow rate of cyclopropane : oxygen 1 3 (50–100 c cm of cyclopropane 300 c cm of oxygen) When the dressing is applied the cyclopropane is turned off and after one or two breaths of oxygen the mask is removed

Endotracheal intubation is used as an aid to the administration of cyclopropane in the following conditions :

(1) Burns involving the face head and neck if the surgeon is to have reasonable access to the parts

(2) Burns involving the dorsal surfaces, when positioning the child makes it difficult to maintain a clear airway

(3) Any child in whom respiratory embarrassment even though minor persists and cannot be relieved by either manipulation or the use of an oral airway

It has been suggested that the introduction of an endotracheal tube narrows the already narrow trachea of a child to a degree which itself causes respiratory embarrassment This premise stimulated the corollary that the largest possible tube should be used and has led anæsthetists to screwing into the trachea uncomfortably large lubricated tubes I believe despite assertions to the contrary that it is the maintained pressure from such tubes that initiates the formation of membranes and post anæsthetic laryngeal œdema reported recently The tube sizes detailed in table V are proportionate to the size of the child they ensure an undisturbed airway and lie comfortably within the larynx With such tubes these dangerous complications do not develop Gentle handling is necessary in introducing the tube particularly in the ill nourished child with infection of the oropharynx but provided the tube is introduced atraumatically I have not found that these factors predispose to laryngeal œdema

It is unnecessary to lubricate the tube Even although atropine has been given the slimy moistness of the child's laryngeal mucosa allows it to slip easily and atraumatically into the larynx

In children aged less than 8 years the vocal cords appear to mould themselves round the tube and an airtight fit is obtained without a pharyngeal pack.

This anæsthetic technique has been used routinely during the past eight years to anæsthetise children with burnt areas ranging from a slight extent to 60–70% of the body surface The results have been most satisfactory The only complication during administration has been an occasional bronchospasm which may be dangerous if not recognised early and rapidly relieved by the application of steady manual pressure to the rebreathing bag filled with oxygen Cardiac irregularities associated with the use of cyclopropane in adults are rarely observed and there have been no cases of postoperative atelectasis

I wish to thank Mr A B Wallace F.R.C.S.E for encouragement and help in writing this article

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# THE TREATMENT OF GENITO-URINARY TUBERCULOSIS

## A REVIEW OF 240 PATIENTS

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Approximately five years ago we commenced an investigation of genito urinary tuberculosis, an investigation based on a unit of 35 beds devoted to this disease at Wrightington Hospital Previous communications (Cosbie Ross, Gow, and St Hill 1951, 1953), together with more recent papers in the *British Journal of Urology* (Ross 1953, Gow 1953) have recorded our earlier experiences The total number of patients treated now amounts to 240, and in this paper we report a new series of 85 and review the earlier groups amounting to 155 We have had the advantage of following up all our previous cases, some of whom first commenced their treatment five years ago The follow up has been carried out with great thoroughness and includes cystoscopy, intravenous and retrograde pyelography, and guineapig inoculation at first six monthly and later at yearly intervals This has naturally entailed a great and increasing volume of work, but the results have been both interesting and encouraging The careful follow up is necessary, not only because of the possibility of tuberculosis developing in another system or organ, but also because a small proportion of the urines may become positive again at the end of two or more years

It can be said at once that the prognosis has greatly improved as a direct consequence of adding chemotherapy to surgery and sanatorium treatment During the first half of this century, using surgery with or without a sanatorium regime, the mortality was approximately 50% Surgery and the sanatorium are still necessary today in the treatment of this insidious disease, but the addition of chemotherapy has reduced the mortality to 10%, and the figure is being improved year by year Our figures include all cases, no matter how advanced or extensive, since all patients with proven genito urinary tuberculosis are accepted by the unit Before chemotherapy some of these patients would have been regarded as beyond hope, and given palliative treatment only

The classification which we use is as follows

| | |
|---|---|
| *Type 1* | early minimal lesion of renal parenchyma |
| *Type 2* | unilateral renal lesion with cystitis and nephrectomy or partial nephrectomy |
| *Type 3* | bilateral renal lesion with cystitis and nephrectomy or partial nephrectomy |
| *Type 4* | cystitis and involvement of the remaining kidney after nephrectomy |
| *Type 5* | (*a*) major bilateral renal disease<br>(*b*) minor bilateral renal disease |

*This is the classification suggested by Jacobs and Borthwick* (1950) but with an additional category of "minor bilateral disease" Even in this modified form the classification is not perfect, but in practice it appears to cover most of the possibilities

We have continued to use thiosemicarbazones in addition to streptomycin, isoniazid, and *p* aminosalicylic acid (P A S ), although in other centres this policy has not received support We have been encouraged *to do so* statement by Domagk in a recent lecture that *strains* bercle bacilli which are resistant to streptomycin soniazid frequently respond to thiosemicarbazone

### Patients Treated Since July, 1952

This group consists of 85 patients (58 males females) 43 presented with renal lesions only, 42 the renal lesions were combined with pul lesions, or bone and joint lesions, or both

The chemotherapy used (Gow 1953) is briefly as

| | |
|---|---|
| Streptomycin 2 g daily, intramuscularly, in 1 dose<br>Isoniazid 250 mg daily orally, in 1 dose | administ fourteen |
| Thiosemicarbazone 100–150 mg daily orally, in divided doses<br>Calcium benzoyl P.A.S 7 g t d s | also admi for fourt |

The two combinations are alternated for a period of months

*Toxicity*

Transient toxic manifestations were caused by mycin in 22 cases, by thiosemicarbazone in 11 cases, P A S in 6 cases There were no toxic reactions to

Toxic reactions to streptomycin occurred in 25% treated, but were always mild and seldom necessita drawal of the drug The main complaints were dizz tinnitus, both of which disappeared a few weeks a course had been completed Toxic effects occurred towards the end of the course, but if they developed desensitisation was carried out by combining the strep with one of the anti histamine drugs ('Phenergan') way it was possible to give all patients a complete

Toxic symptoms due to benzoyl P.A S consisted in nau vomiting, and in 3 patients the drug had to be *Fortunately these 3 patients tolerated the original prep of P A S*

In a few cases the full dose of thiosemicarbazone h reduced to 50 or 100 mg a day because of depress anorexia.

### SURGICAL MEASURES

As we have already emphasised, surgery is as today as before the advent of chemotherapy surgical measures will remain necessary resistant strains continue, and as long as che fails to produce radiographic healing of an ulcer ous lesion In our series any improvement in the ance of the pyelogram has been the exception rat the rule

However, operative treatment should not until the patient has had an adequate period of therapy This will ensure smooth convalesc more important, *enable wounds to heal by firs* This "staging" of surgical measures carried out screen of chemotherapy has almost elimina breaking down nephrectomy wounds of previou

*Nephrectomy*

This operation was carried out in 37 cases paring this figure with the total of 85 it remembered that there was a certain number of tuberculous bacilluria (type 1) and in a few tomy had been done before the patient came care

Our indications for nephrectomy included

(*a*) A non functioning kidney

(*b*) A disintegrated kidney

(*c*) Two focal lesions not located in one pole

(*d*) An ulcerocavernous lesion in the middle a polar calyx and encroaching *on* the hilum

(*e*) "Putty" kidney There is no such autonephrectomy," and these caseous sacs inva apparent active disease when sectioned (Hanley

In all these cases the other kidney was nor only a minor lesion

We have generally found that extensive cal a kidney necessitates its removal, because from the calcified organ remains potentially

*Partial Nephrectomy*

This operation has been made possible only therapy Its advantages over total nephrecto elaboration In particular, it enables bilate measures to be undertaken We have carried hrectomy in 7 cases in the present series the operation isting in removal of the upper or lower pole or of removal of the affected part in a double kidney ral of our patients have had bilateral partial nephrec y In none have we removed the middle calyx but as been shown that this also can be done It is ourse possible to remove an ulcerative lesion and miss by millimetres an adjacent focus, but as Semb 3) has pointed out if the locally destructive lesion emoved the infiltrations usually heal with chemo apy

ie principal indication for partial nephrectomy ars to be an ulcerative lesion of a polar calyx or a lised calcified area combined with a persistently tive urine from the same ureter After partial or plete nephrectomy, our practice is to close the wound out drainage

*nsplantation of Ureter*

e have always been very reluctant to carry out this edure and it appears to be less often necessary now during the earlier years of our investigation In cases a note has been made at the initial cystoscopy owing to the state of the bladder and the severity he frequency transplantation of the ureter into the n would probably be needed later; but usually improvement in the frequency and the degree of bladder healing has made this unnecessary

his is not always so however especially where the rstitial cystitis is pronounced We have carried out nsplant on 5 occasions in the present series and is no doubt that in selected cases the operation has fully justified When the lower two thirds of the r has been extensively diseased we have not hesi to implant the upper third into the descending or the hepatic flexure in each case this has been essful Renal acidosis has been encountered on ral occasions and is nearly always due to neglect on art of an uncooperative patient When the simple involving the constant use of an alkaline mixture salt free diet are combined with periodic analysis blood chemistry little trouble has been encoun When there is a progressive hydronephrosis from ure of the lower end of the ureter we prefer to nt the dilated lower end of the ureter in the fundus bladder provided the condition of the bladder is actory

have carried out nipple ureterostomy (Band 1950) ne of these intractable cases Theoretically nipple ostomy is attractive because it removes the twin rs of ascending infection and renal acidosis more an efficient apparatus for collecting the urine can e provided But while acknowledging its possible in other conditions (e.g., cauda equina lesions) we recommend ureterostomy in renal tuberculosis ureter is diseased as is likely in patients in whom diversion is indicated ulceration and fistula ion occur at the base of the skin nipple We have re abandoned this procedure

*ymectomy*

rculous epididymitis is common and nearly a f our patients had genital lesions We have been sed by the large numbers of patients with a tuber epididymitis combined with type 1 renal lesion idymectomy is apparently not now required as it was two or three years ago It was performed 7 of our 85 patients The operation is however ressary when caseation and abscess formation are and especially if the vas is involved If the mis feels hard or fibrotic it may be safely left on-operative treatment will probably be effective ectomy has not been included in our list of ive procedures because we feel very strongly that utilating operation should not be performed unless the circumstances are quite exceptional It is not an urgent matter to remove the epididymis and especially if there is a large confluent inflammatory mass, there is every advantage in postponing the operation for three or four months while the patient is in the sanatorium receiving a course of chemotherapy If patience is exercised, sufficient improvement will be achieved to enable the operator to find a plane of cleavage between the body of the testis and the epididymis The technique (Ross 1948) involves the extrusion of the testis through a scrotal incision the careful preservation of the blood supply of the body and the bringing out of the stump of the vas through a small stab incision over the external ring

RESULTS

These have been assessed under the following headings (1) sterilisation of the urine (2) clinical improvement and (3) cystoscopic improvement

*Urine*

All were guineapig positive before treatment was begun and of the 85 patients no fewer than 80 achieved a stable negative 5 were unstable but none was persistently positive (table I) 5 had reverted to positive at the end of six months (the longest follow up possible in this group up to the present time) The tubercle bacilli isolated from all positive cultures or guineapig inoculations were tested for sensitivity to streptomycin and isoniazid no strains resistant to streptomycin or isoniazid were isolated

TABLE I—FOLLOW UP OF 85 CASES

|  |  | Urine |  |  |  |
|---|---|---|---|---|---|
| Type | No. of cases | Positive after two months | Positive after four months | Positive after six months | Reverted to positive after six months |
| 1 | 28 | 0 | 1 | 1 | 1 |
| 2 | 34 | 1 | 4 | 1 |  |
| 3 and 4 | 14 | 3 | 0 | [illegible] | [illegible] |
| 5 | 9 | 2 | 1 | 0 | 2 |

1 patient died from advanced pulmonary disease about six months after leaving hospital

For some time we have considered the period of six months chemotherapy to be insufficient —a view which is held by various Scandinavian authorities (Ljunggren 1953) Accordingly we now give in addition a modified course lasting three to six months, after the patient leaves hospital This post sanatorium course is given by the patient's own doctor and consists of

Streptomycin 2 g intramuscularly } twice a week together with
Isoniazid 200 mg orally }
Calcium benzoyl P.A.S. 3 g orally three times a day

*Clinical Improvement*

We have attempted to judge the clinical improvement by the degree of frequency of micturition and nocturia and by the gain in weight Of the 61 patients who originally complained of frequency and nocturia 57 were considerably improved but 4 ultimately required ureterocolic transplant for intractable bladder symptoms 72 patients put on weight the average gain being approximately 1 stone

*Cystoscopic Improvement*

Of the 85 patients 60 had tuberculous cystitis or tuberculous granulations and many had both Of these 50 showed improvement and in 30 the bladder returned to a normal appearance Of 34 with a reduced bladder capacity a considerable increase was recorded in 32.

As in the past we have not seen any improvement in the radiological appearance in the present series

**Follow up of Patients Treated Prior to July, 1952**

93% of the patients treated since 1949 have been followed up (table II) Our aim is to keep as many

TABLE II—RESULTS OF FOLLOW-UP

| Year | No of patients | Died | Given further course of treatment | Positive at end of treatment | Reverted | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | After 1 year | After 2 years | After 3 years | After 4 years | |
| 1949–50 | 51 | 8 following transplant<br>1 advanced pulmonary disease<br>1 severe bilateral renal disease | 3 | 9 | 2 | 2 | 3 | 4 | |
| 1950–51 | 17 | 2 following transplant<br>2 meningitis<br>1 advanced pulmonary disease | 1 | 12 | 5 | 1 | 2 | 1 | |
| 1951–52 | 27 | 1 severe bilateral renal disease | 2 | 1 | 2 | 2 | 1 | 0 | |
| 1952–53 | 30 | 2 severe bilateral renal disease | 2 | 1 | 6 | 2 | 0 | 0 | |
| Total | 155 | 18 (*11 6%*) | 8 (*5 1%*) | 23 (*14 9%*) | 15 (*9 7%*) | 7 (*4 5%*) | 6 (*3 9%*) | 5 (*3 2%*) | |

patients as possible under constant review for ten years from the start of treatment

ANALYSIS OF URINARY INVESTIGATION SINCE 1949

During the present period further efforts have been made to improve our methods for isolating tubercle bacilli from urine In previous investigations we had found that twenty-four-hour specimens did not yield a higher proportion of positive results than early morning specimens In an attempt to improve the twenty four-hour specimen results, the volume of urine from which a sediment was obtained after forty eight hours' standing was increased, firstly to 250 ml and secondly to 750 ml Table III shows that increasing the volume of twenty four-hour urine specimens did not increase the number of positive results We believe that several factors account for this

In the first place, twenty four hour specimens are collected at intervals in the ward and are open to many contaminants, including moulds and bacteria relatively resistant to the action of sodium hydroxide Many specimens have accordingly to be treated twice with sodium hydroxide, which doubles the risk that the sodium hydroxide will kill the tubercle bacilli as well Secondly, most twenty four hour specimens develop large amounts of phosphatic and other deposits, which impede the action of the sodium hydroxide, and lead to the production of bulky and unwieldy material for final inoculation We have consequently abandoned using twenty four hour specimens, believing that the results from early morning specimens are equally good The results of the first 200 early morning specimens have been compared with those of the preceding twenty four hour specimens (table IV) There was no significant difference between the early morning and twenty four hour specimen results, and the results from artificial culture were as good as from guineapig inoculation It was noteworthy that the number of positive results obtained when the two methods were combined was consistently higher than when either method was used alone

TABLE III—EFFECT OF INCREASING VOLUME OF URINE CENTRIFUGED

| Vol centrifuged | No tested by artificial culture | No positive | No tested by guineapig inoculation | No positive |
|---|---|---|---|---|
| 100 ml | 441 | 20 (*5%*) | 284 | 68 (*24%*) |
| 250 ml | 230 | 16 (*7%*) | 230 | 60 (*26%*) |
| 750 ml | 119 | 28 (*7%*) | 419 | 50 (*12%*) |

Sodium hydroxide, which we used to destroy contaminating organisms in our specimens, is reputed to kill tubercle bacilli as well as contaminants We therefore incorporated chloramphenicol in the Löwenstein-Jensen medium, in the hope that it would suppress the growth of contaminants and do away with the need for using sodium hydroxide All specimens from which no growth was obtained on a preliminary overnight culture on blood agar (containing 10 µg of chloramphenicol per gramme of medium) were inoculated on to Löwenstein media without any further treatment We found ause of the lability of chloramphenicol 100 µg had lded to each gramme of Löwenstein Jensen medium to suppress contaminants for six weeks At this growth of the tubercle bacilli themselves was inhibited

We therefore reduced the time that the sodium hyd (3%) remained in contact with the urinary deposits twenty minutes to five minutes We found that five m was long enough to decontaminate practically all our s mens, but that the proportion of positive tubercle b cultures was not increased by the shorter time From follows either that 3% sodium hydroxide is not let tubercle bacilli immersed in it for twenty minutes, o lethal effect is not lessened by shortening the time o

TABLE IV—COMPARISON OF CULTURE METHODS

| Specimen | No of specimens | No positive by artificial culture | No positive by guineapig inoculation | Com no po |
|---|---|---|---|---|
| Early morning | 202 | 19 (*9 5%*) | 19 (*9 5%*) | 28 (*1 |
| 24 hour | 419 | 28 (*7%*) | 50 (*12%*) | 54 |

The technique we now employ is

The early morning specimen is collected and diately to the laboratory, where the whole of it is for half an hour at 2000 r p m , the deposit is tre 3% sodium hydroxide at 37°C for five minutes, ne centrifuged for twenty minutes and the resultant inoculated on to two Löwenstein Jensen plates an guineapig

TREND OF RESULTS

The over-all figures for the proportion of isolations of tubercle bacilli from urinary s received during the last three years are given in In the early stages the proportion of positive res high this was to be expected, for many from untreated cases As the trial proceeded, the tion of treated to untreated cases rose steadily, was reflected in the steady fall in the number of guineapig results The proportion of positive obtained by artificial cultures, on the other hand diminish consequently, while guineapig inocu first gave better results than artificial culture, both methods gave very similar results The ex probably lies in the improvements which we mad technique over the past three years the tu in our final deposits are now in sufficient n allow growth on artificial culture media as guineapigs Each method will of course which explains why the combined results are b those of either method taken individually (table

TABLE V—RESULTS FOR LAST THREE YEARS

| Specimen | No tested by artificial culture | No positive | No tested by guineapig inoculation | N |
|---|---|---|---|---|
| Early morning | 765 | 82 (*10 5%*) | 559 | 49 |
| 24 hour | 1297 | 78 (*6%*) | 962 | 184 |

### Discussion

e have been concerned by the emergence of resistant ns of organisms in a small number of patients ed in earlier groups In some of these the resistant nisms have been found when a previous course of ment often inadequate, has been given elsewhere void this difficulty we have for some years given the drugs in pairs alternately for two weeks at a time bove) By this means not only are resistant strains less likely to occur but toxicity is reduced to a num. Further, it is now well established that zid and streptomycin given together are much effective than either given alone (Mackaness 1953) e is no place in the treatment of genito urinary culosis for prolonged administration of a single

cently there was reported the result of a clinical trial e United States of America of an isoniazid derivative 213) Although this new preparation is weight for it slightly less active than isoniazid it appears to be t one-tenth as toxic (Bavin et al. 1952 Katz et al For patients who fail to respond to streptomycin and azid or who have become resistant to one or both s we have recently instituted an alternative course sting of 1 5 to 2 0 g of H P 213 combined with vio n 2 g a day The combination is given for periods ortnight, alternating with fortnightly courses of thio carbazone and calcium benzoyl P.A.S Viomycin has given with caution because of its toxicity, but using method of intermittent dosage we have not so far any trouble A careful watch for the appearance of nin is especially important

have been encouraged to learn that other workers lvising long intermittent courses of treatment for ulosis of other organs (Joiner et al 1954) We have tently advocated this policy for a number of years

*cted Bladder*

ere tuberculous cystitis may often heal completely ay leave the patient with troublesome residual oms of frequency and nocturia due to a contracted r Superficial cystitis heals well, but interstitial s may leave a diminished capacity Thornley suggested that cortisone might be useful in these and we have therefore treated a small series with f cortisone spread over a period of four weeks. was administered daily for two weeks, followed by daily till the whole gramme had been given Only s in whom the disease had been inactive for some ave been considered suitable for this form of ent So far results are not encouraging

*sive Hydronephrosis*

ur experience patients with progressive hydro sis usually do not improve, and we have not had success with such simple measures as ureteric on (Lane 1954) It is often difficult to pass a catheter in these cases, and subsequently, at on we have found the lower third of the ureter lod in a solid mass of fibrous tissue When only er third of the ureter is involved it may be possible ant the upper end into the bladder fundus If r there is tuberculous cystitis and if much of ter is involved a ureterocolic transplant is best out

*cy and Genito urinary Tuberculosis*

present policy is to allow the pregnancy to con rovided the renal disease is not widespread and l also that the lungs are not much involved If on is of minor degree a normal confinement is ed, the chemotherapy dosage being reduced by ing the last few months of pregnancy Frequent tions of the urine for albumin are necessary s advisable to carry out intravenous pyelography once or twice to make sure that the minor renal lesion shows no signs of spread. Should spread occur it is advisable to terminate the pregnancy forthwith

### Summary

We have continued our investigation of genito urinary tuberculosis Another 85 cases are discussed.

The 155 patients of our earlier series, some of whom began treatment in 1949 have been regularly followed up The results are reviewed

It was found that these patients had to be followed up indefinitely since the urine reverted to positive within twelve months in 9 7% and within two years in 14 2%

Further experience confirmed our belief that anti tuberculous drugs should always be given in combination and that the intermittent method of therapy offers great advantages

Further experience also convinced us that the course of treatment should be continued up to a year, and even longer

A new course was used in patients with strains of organisms resistant to the usual drugs

By combining surgery and a sanatorium régime with modern chemotherapy the prognosis has been greatly improved

We should like to thank Mr J Dobson consultant surgeon superintendent Wrightington Hospital for his help and cooperation Prof D T Robinson who was responsible for the guineapig inoculation tests and Smith & Nephew Research Ltd. for technical assistance and supplies of isoniazid thiosemicarbazone benzoyl P.A.S and H.P 213 We are grateful also to Mrs C. Wilding who carried out all the technical laboratory work, and to the medical research committee of the board of governors, Liverpool United Hospital who have provided one of us (J G G) with a grant to assist this investigation

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No one can prevent young people asking questions—the same awkward questions—of the generation that precedes it. My greatest hope I think, lies in this restless searching for satisfactory answers that goes on in young people's minds before they lapse into the acceptance that tends to come with age for by it truth can be reborn. Nothing can still this unquiet pulse Between the ages of perhaps fifteen and twenty five we question and establish our fundamental beliefs In the future I think we must somehow seize the exciting opportunity this gives In the lifetime of each person this chance comes only once Is it not possible to encourage in our youth a love of hardship adventure and effort to give greater training in service and citizenship so that later a spontaneous awareness arises of problems at home and abroad of religion and of politics ? This enquiry may lead to one religion, to another religion or even to no religion It may lead to one political party another political party or to no political party But at any rate I believe it will strengthen in all of us a conviction of the value of individual freedom and unless we know its value we cannot defend it —Dr ROGER BANNISTER, *The Listener* 1954 52, 1141

# CHRONIC BRONCHITIS

## AN ATTEMPT TO CONTROL CHRONIC INFECTION WITH HÆMOPHILUS INFLUENZÆ BY AEROSOL THERAPY

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In chronic bronchitis there is colonisation of the bronchial tree by nasopharyngeal bacteria (Stuart-Harris et al 1953), which may be classified into two groups (May 1953)

(1) "Pathogens" pneumococcus, *Hæmophilus influenzæ*, *Staphylococcus aureus*, group A hæmolytic streptococci, and Friedländer's bacillus

(2) "Non pathogens" *Streptococcus viridans*, non hæmolytic streptococci, diphtheroids, *Neisseria catarrhalis*, and *Staph albus*

During the summer months and between exacerbations in the winter one or more of the "non-pathogenic" bacteria usually predominate in mucoid sputum, although pathogens may be present in small numbers During this phase antibacterial drugs temporarily reduce the number of bacteria and of inflammatory cells (Elmes et al. 1953) but have very little clinical effect During an exacerbation there is proliferation of one of the "pathogens," usually either a pneumococcus or *H influenzæ*, and the sputum becomes purulent, but we have observed that this may follow the onset of clinical symptoms in some instances, hence the bacterial infection may be the consequence rather than the cause Antibacterial drugs given during an exacerbation suppress the "pathogens," the sputum becomes less purulent, and there is usually clinical improvement

Reid's (1954) pathological studies suggest that during these exacerbations, while the bronchioles are temporarily occluded, permanent damage may be caused to the lungs by extension of inflammation to the lobules Presumably the bacteria concerned belong to May's "pathogen" group, therefore their suppression during an exacerbation should both reduce its length and severity and delay the gradual deterioration of lung function which is characteristic of this disease Prophylactic treatment to prevent proliferation of these bacteria should be directed particularly against *H influenzæ*, since the drugs to which it is sensitive will also suppress pneumococcal infections

Systemic penicillin, in doses likely to be tolerated over long periods, encourages the proliferation of *H influenzæ* Of the "wide spectrum" antibiotics chloramphenicol is the most effective against *H influenzæ*, but its effect is only temporary, and long term administration is precluded by its toxicity Combinations of streptomycin and penicillin have been advocated by Mulder et al (1952), but constant systemic streptomycin is impracticable for the treatment of large numbers of bronchitics apart from the danger of damage to the labyrinths from the doses needed We therefore tried local therapy with streptomycin and penicillin in patients with chronic *H influenzæ* infections to see whether such therapy could be applied effectively for long periods without serious complications such as sensitivity to the drugs and a serious proliferation of insensitive organisms Although theoretically promising, this method did not prove
le in a pilot trial made on a small group of inpatients
utpatients, which is the subject of our present brief

## Material

Details of the cases are given in table I The inpatients (cases 1–3) had been admitted with exacerbations of their chronic bronchitis and were to have a predominant growth of *H influen-* sputum The six outpatients were not acutely ill treatment was started but were less well than th been in the summer All were known to have predominant infection with *H influenzæ* for at month, some for more than a year, and they ha under observation during the preceding winter had received chemotherapy within a month of th of the trial

## Methods

*Clinical Assessment* —With the exception of the outpatients attended weekly, and their was assessed by standard questions and clinical tion Case 4 was seen less frequently but sent specimens of sputum and progress reports

*Treatment* —The dose of penicillin G and sulphate was dissolved in 1 5 ml of 0 5% sulphate This was dispensed in rubber sealed containing a week's supply and retained its at room-temperature over this period The measured out the dose with a 2 ml syringe and

TABLE I—DETAILS OF CASES

| Case no | Age (yr) | Sex | Grade of dyspnœa at best (Fletcher 1959) |
|---|---|---|---|
| *Inpatients* | | | |
| 1 | 74 | M | 4 |
| 2 | 67 | F | 4 |
| 3 | 63 | M | 2 |
| *Outpatients* | | | |
| 4 | 61 | M | 1 |
| 5 | 64 | M | 1 |
| 6 | 56 | M | 2 |
| 7 | 57 | M | 3 |
| 8 | 62 | M | 4 |
| 9 | 60 | M | 4 |

electrically driven 'Deedon' plastic inhaler with mask They were instructed to gargle and to faces and hands after each treatment to dimi risk of skin sensitisation The inhalation from fifteen to twenty minutes All the outpatie using a hand spray to administer compound and atropine spray (*N.F*), when necessary, to bronchospasm

*Bacteriological* —The techniques of mechanical genisation, culture, and viable counting were described by Elmes et al (1953) Gutters for mycin sensitivity testing contained 200 µg streptomycin, and the control organism was *aureus* To facilitate the identification of *H* 0 2 unit of penicillin per ml was incorporate chocolate agar medium The streptomycin homogenised sputum was estimated by the me by Mitchison and Spicer (1949) for serum fluids The lowest level of streptomycin which detected by this method is 1 µg per ml The Abraham et al. (1941) was used for the esti penicillin, except that agar seeded with the staphylococcus before pouring was used in surface inoculated medium

*Microscopical* —Sputum smears were analysed by the method described by Elmes et al

## Results

The inpatients were used to determine what penicillin and streptomycin should be given method

*Inpatients*

**Case 1** was given penicillin 200,000 units and str 0 2 g twice daily, and specimens of sputum taken were cultured and tested for the presence of pen

TABLE II—RESULTS OF TREATMENT

| Effect of treatment on *H influenzæ* in sputum | Exacerbations | | | | |
|---|---|---|---|---|---|
| | During treatment | | After treatment | | Previous winter |
| | No and severity | Change in flora | Interval and severity | Change in flora | |
| *tients* | | | | | |
| Eliminated | None | | 3 weeks moderate | *H influenzæ* already present | 1 severe |
| Slight reduction | None | | 3 weeks severe | *H influenzæ* already present | 1 severe |
| Eliminated | None | | 1½ hr severe | *H influenzæ* returned later | None |
| *atients* | | | | | |
| None | 1 mild | None | None | | None |
| None | 1 severe | None | None | | 1 severe* |
| None | 1 mild | None | 5 weeks moderate | Increase in no of *H influenzæ* | 1 moderate |
| Temporary reduction | 1 mild | None | 3 weeks severe | None | 1 mild 1 moderate |
| Eliminated | None | | 4 days moderate | Reappearance of *H influenzæ* | 1 mild, 2 moderate |
| Eliminated for first 2 months, then returned to previous level | 1 moderate | Pneumococcus appeared | 10 days moderate | None | 2 mild* |
| | 1 moderate | None | | | |

Despite courses of chemotherapy

tomycin The sputum contained an effective level of cillin (8 units per ml ) twelve hours after the start of tment but streptomycin was never detected During the three days *H influenzæ* was found occasionally in the um; hence antibiotic cover was not being provided ughout the twenty four hours of each day but after the th day of treatment all the specimens collected before the *ning treatment contained no H influenzæ By the end of* first day the sputum had become mucoid and its volume progressively until after the third day it was only possible btain a small morning specimen Treatment was continued ten days. Five days later *H influenzæ* reappeared in the um in large numbers, although the character of the um hardly changed and the patient s clinical condition nued to improve until the time of discharge a few days

Seen as an outpatient a month later his condition had iorated and he was again coughing up large volumes of ent sputum yielding a profuse growth of *H influenzæ*

se 2 was too ill to coöperate well in taking the inhalations reptomycin 0 5 g and penicillin 200 000 units twice daily fection was only partly controlled When the dosage ncreased the antibiotics tended to crystallise out in haler and the treatment became even less effective. nfection responded well to parenteral penicillin and tomycin

se 3 —Despite a predominant growth of *H influenzæ* atient was producing a large volume of mucoid sputum treatment was started with penicillin 500 000 units and omycin 1 g twice daily Initially difficulty was caused ugs crystallising out in the vehicle but this was pro l by adding distilled water After this had been done *luenzæ* disappeared from the sputum which decreased ume and became less cellular The treatment was ined for twelve days, during the last four of which *monas pyocyanea* appeared in the sputum in moderate rs without any clinical or microscopic change Within hours of the last treatment the patient developed n and increasing dyspnœa, but it was not until three days hat his sputum became purulent and *H influenzæ* ared. He was by then desperately ill was treated with nphenicol cortisone and Alevaire and recovered. phils did not appear in his sputum until he had been isone for three days; therefore it is unlikely that the nation was due to sensitivity to the aerosol There change in this patient s agglutination titre to the n pathogenic respiratory viruses at this time (The test ide by the Virus Reference Laboratory Colindale )

*ients*

vas decided to give the outpatients penicillin ) units and streptomycin 0 4 g in 1 5 ml of vehicle laily

results are summarised in table II which shows *influenzæ* was satisfactorily eliminated from the n only in case 8 who was also the only patient in exacerbation of his bronchitis during treatment utum always contained large numbers of poly but was not grossly purulent His relapse utely after the cessation of treatment was associated with the reappearance of large numbers of *H influenzæ* in his sputum indicating that this infection had been suppressed rather than eradicated He responded to a further course of penicillin and streptomycin inhalations but relapsed again when this was stopped

An exacerbation was defined as a sudden clinical deterioration with pyrexia and breathlessness causing the patient to stay in bed for two or more days Such exacerbations developed during treatment in all the other outpatients, but only one (case 9 first exacerbation) was associated with a change in flora This took place when *H influenzæ* could not be cultured from the patient s sputum and when his inhaler was out of order it was associated with the proliferation of a pneumococcus and responded to further inhalations and parenteral penicillin

All the other exacerbations took place while *H influenzæ* was present in the sputum although not necessarily in large numbers Since *H influenzæ* did not proliferate significantly with the exacerbations it seems unlikely to have been the cause

### *Bacteriology*

Total viable counts on the specimens from the inpatients in whom the treatment was effective showed a reduction from $10^6$ to $10^4$ bacteria per ml in case 1 and to zero in case 3 This reduction lasted about three days and then the total count increased rapidly to the pre-treatment level even though the pathogen was still absent. Viable counts on the outpatients done weekly for the first two or three weeks showed no significant change and were not continued There was no significant change in the flora other than those mentioned above

### *Microscopy*

As in our previous study the microscopical findings in the sputum showed a good correlation with the clinical state of the patient During exacerbations the polymorphs and deoxyribonucleoprotein fibres increased at the expense of the mucoprotein but when the sputum was mucoid between exacerbations although it might contain no deoxyribonucleoprotein fibres the neutrophil polymorph was still the most numerous cell Eosinophils were present from time to time in the sputum of all the patients but seldom in greater proportion than 5% of the total cells present; their presence was not correlated with any clinical symptom or sign

### *Side-effects*

No evidence of either cutaneous or bronchial allergy developed in any of the patients although there were occasional breaks in therapy of up to a week due to mechanical failures No disturbance of gastro-intestinal function nor any other side-effect was noted The patients found the inhalations tasteless.

### Conclusions

Our conclusion is that our method of administering penicillin and streptomycin as an aerosol cannot be relied on to control bronchial infection by *H influenzæ* Furthermore, even the one case in which the infection was controlled for as long as six months relapsed immediately after the treatment was stopped The reason for the failure of the method in five out of six patients is not clear, because the persistant organisms retained their original sensitivity to penicillin and streptomycin Perhaps the uneven distribution of an inhaled aerosol in emphysematous patients permits foci of infection to persist in parts of the lung to which the aerosol does not penetrate

Our observations support the view that *H influenzæ* is of importance in severe chronic bronchitis We have already shown (Elmes et al 1953) that patients infected by this organism appear more susceptible to the effects of fog than those without it, and in our present small series only the patient whose infection was controlled escaped an acute exacerbation while the treatment continued The exact rôle of *H influenzæ* in chronic bronchitis remains obscure Although exacerbations occur more frequently when it is present, they are not always associated with proliferation of *H influenzæ*, nor does a proliferation of this organism necessarily cause a clinical exacerbation

### Summary

An aerosol of penicillin and streptomycin was used in an attempt to suppress *H influenzæ* infections in nine patients with severe chronic bronchitis

It was successful in three of them with clinical benefit

In the others *H influenzæ* persisted in the sputum, and they had winter exacerbation of their bronchitis

The bacteriological and clinical findings are described

We wish to thank Dr S Sherlock and Dr R I S Bayliss for permission to treat their inpatients, members of the staff of the departments of medicine and bacteriology who made some of the observations when we could not do so, Miss M Burton for preparing the solutions for inhalation, and Moore Medicinal Products Ltd for the loan of the electrically driven Deedon inhalers

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# HEART-FAILURE FROM RETENTION OF SALT AND WATER CAUSED BY TREATMENT WITH PENTAPYRROLIDINIUM BITARTRATE

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DURING the past fifteen months we have been treating with pentapyrrolidinium bitartrate (' Ansolysen '), usually by mouth, about 100 patients with severe hypertension The results much resemble those obtained by Smirk (1953)

The patients included several who had symptoms of heart-failure before treatment, and usually these symp[illegible] soon disappeared It was therefore especially [illegible]ble that during treatment 2 patients with relative failure developed symptoms of absolute failure, with œdema and dyspnœa at rest Moyer and Mills ( have shown that after the administration of a singl of hexamethonium the renal excretion of wate sodium chloride decreases The same applies to pyrrolidinium I therefore tried to find out i symptoms of heart-failure were due to this retenti salt and water

### Investigation

5 of our hypertensives were given a diet containing about 8 g of sodium chloride They received this diet for eight days before treatment, and for the first two or three treatment During this time the daily urinary ex of sodium, potassium, and chloride was measured. P pyrrolidinium bitartrate was injected hypoder thrice daily at 7 A M, 2 P M, and 9 P M The init was usually 1 25–2 50 mg, and the dosage was gradually as the patients became habituated The b pressure in the erect and recumbent postures measured thrice daily at 8 30 A M, 12 30 P.M, 6 P M

The urinary excretion of sodium chloride in all the patients at the beginning of the tr but the degree of retention varied much from one p to another 1 patient developed symptoms resembling those of cardiac asthma

**Case 1** —A housewife, aged 62, had had for many years During the past year she had had dyspnœa on slight exertion, such as ordinary walking had never had dyspnœa at rest or cardiac pain She was dizzy, and her memory was poor

*On examination* she was somewhat overweight, with of the lips and slight dyspnœa at rest On auscultation lungs there was slight basal crepitation, respirat vesicular The heart was enlarged, its action was and a systolic murmur was heard over the aorta The was obese The liver was not palpable, and there ascites There was slight œdema of the ankles Blood on admission was 270/145 mm. Hg

*Laboratory Investigations* —Hæmoglobin 93–91% cyte sedimentation rate 20 mm in 1st hr, blood urea per 100 ml The urine contained no blood, protein, sp gr 1 007–1 018 Electrocardiography showed T waves in the first and second leads, and left axis Radiography showed considerable enlargement of especially to the left There was no pulmonary

*Treatment and Progress* —During the whole of her hospital the patient was given a diet containing of sodium chloride daily Since, after a week in her blood-pressure was still about 225/140 mm. Hg the erect and the recumbent postures, hypodermic ad tion of pentapyrrolidinium bitartrate was institute initial dose was 1 25 mg t i d, increasing to 6 25 mg she developed tolerance During the first few days, the felt well, and her blood pressure was about 170/10 in the erect posture However, after twelve days' tr she began to feel tired again, and on the fourteenth treatment she woke in the morning with dyspnœ subsided spontaneously On the fifteenth day she c lie down, owing to pronounced dyspnœa, which present in the sitting posture Moist râles were hear on auscultation of the lungs, and considerable œde ankles had developed Her blood pressure was factory, about 145/100 mm Hg, but, since her dition had apparently been caused by the treatment discontinued The dyspnœa became worse in the co day, so in the evening we started treatment with diuretics A profuse diuresis occurred during the next morning the patient felt much better, she then slight dyspnœa at rest Treatment with was resumed, this time by mouth, and a mercuria was given once a week During the past month has felt well, her blood pressure is about 170/105 in the erect posture, and 185/115 mm. Hg in the r posture Fig 1 shows the patient's weight, Hb and urinary excretion of sodium and chloride shows that considerable hydræmia developed dur ment The excretion of sodium chloride before treatment shows that the patient retained about

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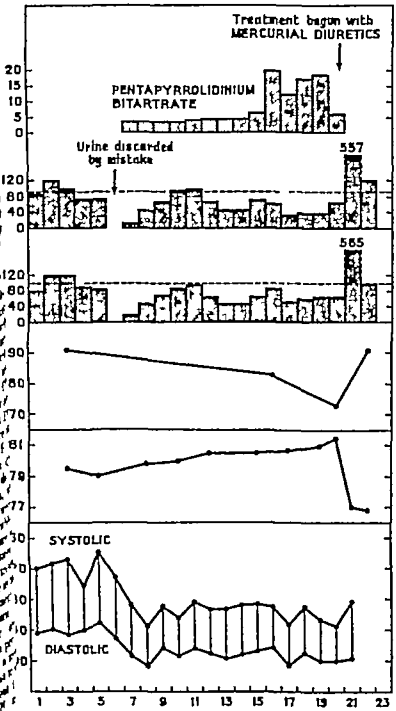
Aided by a grant from P Carl Petersen's Foundation substance Her weight increased by 2 5 kg and, since received a low calorie diet at the same time it can be n for granted that at least 2 5 kg of water was retained the other hand the urinary excretion of potassium was slightly influenced except that it was somewhat decreased ng the first two days treatment.

efore treatment this patient was on the border of plute heart-failure but it was undoubtedly the ntion of salt and water caused by pentapyrrolidinium caused her cardiac asthma

he 2 above-mentioned cases with similar symptoms ch were responsible for this investigation into the ary excretion of salt and water during treatment with apyrrolidinium were as follows

ase 2.—A housewife aged 61 with severe hypertension and ertensive heart-disease Six days after admission her d pressure was still about 230/140 mm. Hg oral treat t with pentapyrrolidinium bitartrate 20 mg four times y was therefore instituted After twenty three days ment she was discharged with instructions to take ng four times a day Except for some fatigue she felt then. Since the beginning of the treatment she had ased her weight by 6 kg A fortnight after discharge was readmitted owing to great fatigue dyspnœa on tion and increasing abdominal circumference. Examina now showed that she had congestion of the lungs and iderable ascites; since the start of treatment five weeks er her weight had increased by 11 0 kg and her Hb decreased from 93 to 78% (hydræmia) We continued treatment but administered mercurial diuretics also ing this regimen the patient lost 15 4 kg and her Hb



Hæmoglobin body-weight, blood-pressure and urinary excretion of chloride and of sodium in case 1

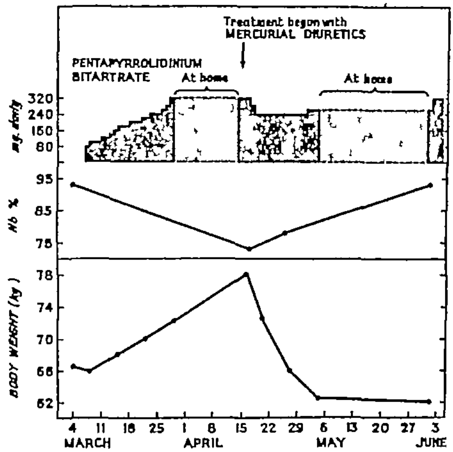


Fig 2—Hæmoglobin and body-weight in case 2. Note hydræmia accompanying increase of weight.

increased to its previous values. Since then she has felt well during three months continued treatment with pentapyrrolidinium combined with injections of mercurial diuretics once or twice weekly Her blood pressure is about 180 120 mm. Hg in the erect posture and 210/120 mm. Hg in the recumbent posture Fig 2 shows her weight and Hb values during treatment

**Case 3**—A hospital nurse aged 52 with considerable hypertension and mitral stenosis. Oral treatment with pentapyrrolidinium exerted a beneficial effect on her headache and dyspnœa on exertion, but the effect on her blood pressure was somewhat fluctuating and several times she developed symptoms of overdosage—dizziness and vomiting At the same time she had slight dyspnœa at rest, tickling cough, and signs of pulmonary congestion on auscultation These symptoms always subsided when the dose of pentapyrrolidinium was temporarily reduced

Even though the salt and water excretion before and during treatment was not investigated in these two cases there can hardly be any doubt that the symptoms in both cases were due to salt and water retention caused by the treatment with pentapyrrolidinium

### Discussion

During treatment of hypertension with pentapyrrolidinium some water and some salt are retained in the organism. The cause of this is not yet known Pentapyrrolidinium may possibly influence the kidneys directly but it is also possible that the reduction in the blood pressure prevents an affected kidney from excreting salt and water The latter probably plays at least some part for in the case of intravenous administration of veratrum preparations a pronounced antidiuretic effect is also observed (Freis et al 1949 Meilman 1953) in spite of the fact that the reduction of blood pressure by the veratrum preparations is chiefly of central origin whereas that produced by the methonium preparations is due to ganglionic block

Similar cases during hexamethonium treatment have not been reported hitherto but Persson (1951) has observed an increase of the patient s weight in several cases during hexamethonium treatment and I have observed the same Owing to the rather short duration of the effect of hexamethonium it is difficult with this form of treatment to keep the blood pressure effectively lowered throughout the twenty four hours and this may be the reason why the retention of salt and water is not enough to give rise to alarming symptoms

In our department we have seen severe symptoms in 3 of about 100 hypertensives treated with pentapyrrolidinium, *and in several others we have seen a* transient tendency to œdema at the beginning of the treatment This is of no slight practical importance, this retention of salt and water is not harmless, since, as shown by the cases cited here, it may give rise to alarming symptoms In such cases unawareness that pentapyrrolidinium causes retention of water and salt may lead to continued treatment, which may be useless or even harmful, but it should be possible to avoid these symptoms of circulatory disturbances by relatively simple measures The following rules should be observed

(1) During the early part of treatment every hypertensive treated with pentapyrrolidinium should be weighed twice a week.

(2) If the patient's weight increases considerably during treatment, he should be closely observed, and, if symptoms of decompensation develop, mercurial diuretics should be administered, or else the dose of pentapyrrolidinium should be reduced

### Conclusion

The treatment of hypertension with pentapyrrolidinium causes retention of salt and water in the organism In a few cases this retention may cause latent heart failure to become manifest, as hydræmia, pulmonary congestion, dyspnœa at rest, and œdema develop, but in the great majority of cases it produces no symptoms My 3 patients were on the border of incompensation already before treatment, so possibly it is only in such patients that pentapyrrolidinium may produce symptoms of circulatory stress

This condition is undoubtedly not harmless, especially if it is not recognised The treatment can, however, be completed either by combining pentapyrrolidinium with mercurial diurectics (cases 1 and 2) or by reducing the dose of pentapyrrolidinium (case 3)

### Summary

The treatment of hypertension with pentapyrrolidinium causes retention of salt and water

In some cases this retention of salt and water may cause relative heart-failure to become absolute This happened in 3 of about 100 hypertensives treated with pentapyrrolidinium All 3 patients were on the border of incompensation before treatment

Such cases can be found by frequently weighing the patient in the early stages of treatment, and this trouble some complication may be avoided by administering mercurial diuretics or by reducing the dosage of pentapyrrolidinium

Messrs May & Baker Ltd supplied the pentapyrrolidinium *compounds*

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" Big buildings are not new But in the big buildings of tradition—the churches, the castles the city halls—it was each part that was big, and the impressiveness of the architecture depended on this Moreover, the large elements in the design represented large spaces inside Our new, big buildings are different They are composed of relatively small parts multiplied almost indefinitely And the spaces inside them are small The repetition of more or less identical smallish units—flats or offices—is expressed externally by rows and tiers of identical windows Not only do these threaten a new monotony, but the swollen bulk of the buildings has a destructive effect on the townscape, all the more disturbing because their purpose—housing, finance, adminis n—does not entitle them to dominate over their dings as cathedrals and courts of justice—the symbols l organisation—can legitimately dominate over theirs "

RICHARDS *Listener*, Jan 6, 1955 p 18

# IMPOTENCE

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SEXUAL impotence is generally regarded as a logical disorder, but it can be satisfactorily tre methods that are essentially *physiological.* To that it is caused by a failure in emotional relati and that treatment should be directed to a these relationships, is, I am sure, unwise

### Classification

There are only three ways in which sexual may fail (1) insufficient erection (in strength, fre *or duration*), (2) *premature ejaculation*, absence of ejaculation

### Erectile Impotence

*Causes*

Many people think that there is some a between men and women which should arouse th sexual desire at appropriate times, and that t something wrong with them, or their wives, desire is not kindled But the truth is that the stimuli to erection are all through contact Adu with growth and experience, and the conditioned reflexes, erotic sensation may be by a wide variety of stimuli and by *fantasy* basic stimulus is that of touch

Under natural conditions a young man nev intercourse His first contact with a woman casual or deliberately exploratory, but he step by step, by his urge for more satisfying stimuli, until he reaches a point when inter inevitable

*In a civilised society restrictions* are *placed* intercourse, opportunities for physical con reduced and the natural development of th instinct is thus delayed In theory developmen proceed naturally when restrictions are *rem* matrimony, but in fact marriage too often " must not " overnight to " must," and, thoug can at any stage say " I won't " without harm to he can never say " I will " without the risk, later, of failing

Nearly all the *failures can be traced* direct or other of our faulty cultural patterns Th represents sexual intercourse as a contest betw and woman, in which the aim may be said gain the highest score Another elementary there is a " right " type and amount of sexua for different periods of life and that those wh from it damage their health At a higher cult —*that of marriage manuals*—intercourse complicated psychophysical skill

Highest of all is the spiritual pattern and its shadow which ignore the physical aspect of teach that the act has no significance unless it panied by a spiritual or psychological union concerned here only with the physiology of with the use made by, or meaning given to any participants, but I must offer my when function is inhibited by *consciousnes* absence of exaltation, it is more likely to b by, so to speak, working from below *upwards* above downwards

*Treatment*

When intercourse has failed, the patient trying and retrace the steps of courtship, whic cases he may never have trod at all Most couples, in order to avoid a humiliating *situa* sensibly spend as little time as possible in *bed* the first problem is to persuade them to spend n time in bed together for spontaneous contact e place At the start a man cannot help feeling very contact is a signal for an attempt at inter and, as he does so his attention is diverted from nsual pleasure to its probable outcome and the il reflexes are inhibited proportionately After a he search for pleasure becomes his objective and gets that he is trying to achieve intercourse and g as he is occupied in exploring appreciating and ving on his contact sensations and perhaps inter ng them with erotic fantasies he cannot be worrying his impotence

h is the margin of potency in young men that many regular intercourse for years without being aware y sensual pleasure—the activity being kept on habit or a sense of obligation But in these circum s desire wanes early and when they come for nent they must still be retrained on the same lines ssence of treatment is the simple lesson that inter e is a sensual pleasure or nothing

st endocrinologists maintain that testosterone is olpful in cases of functional impotence On the hand erectile capacity is not a constant but is ed by stress worry or failure, and in such cases ncreased by giving testosterone

ll four years ago I used methyltestosterone by mouth esponse in about half the cases but since then I have implantation and in every case some improvement in on has followed. The effect of sublingual tablets is stant and even in the patients who respond it declines y are taken regularly In order to take a dose that may ective the man must decide some hours in advance when ll make an attempt and planning is the main thing I avoid

ming erections can be regarded as a reliable indication otile capacity being independent of the sexual situation, n every case where these are depressed I give an implant tween 100 and 200 mg of testosterone I insert 25 mg nts (2 2 mm. diameter) with a trocar and cannula th the skin on the outer aspect of the thigh using ml of Novutox for local anæsthesia No stitch uired.

eral of my patients who have had injections of testo ho elsewhere have reported that there was no response them, or that the response was too transitory to be of se

### *al Features*

no patients have had sexual fantasies or activities many would call perverted Inquiry for these l be made as a routine and since some men onceal such facts unless put completely at their have learnt to frame my questions in an encourag y The patients usually feel that their fantasy is abnormal and make a big effort to abandon it and ch their wives in a spirit of what they regard as love. However the fantasy may be so closely into their sexual reflex that they only succeed biting all sexual response

48 patients in this category whom I have seen een only masochists mild sadists fetishists and stists and I have told them that I think their fall within the normal range of variation I have them to keep their fantasies and bring them their ordinary sex contacts and I have made it at once satisfactory intercourse is established the s will fall into the background I was at first ed and disappointed at the success of this approach ntended only to give them first aid relief in a to situation and then settle down to learn ng of their individual psychopathology But now satisfied that such first aid is all they

ust be difficult for a man however good his lity to integrate a trait that is taboo in his section of society I cannot hold that because the effort to do so has caused a transitory loss of potency he therefore has neurosis Any quality that lies at an extreme of the range of variations may cause its possessor certain difficulties and the treatment of these patients consists essentially in widening their concept of the normal range of human qualities

## Premature Ejaculation

### *Cause*

This condition typically occurs in young well sexed men at the start of their marriage but occasionally it is the chief complaint of a man whose erections are failing and in these cases the treatment is that of erectile failure The usual story is that as a boy the patient had a strong urge to masturbation (The actual stated frequency is not significant because one cannot estimate the degree of restraint that he has exercised This restraint, which psychiatrists call "guilt" is usually based on by current standards perfectly reasonable moral scruples or on considerations of health or athletic prowess ) There was probably an ardent courtship, with involuntary ejaculations even on clothed contacts and, if there were attempts at intercourse before marriage they ended in a premature ejaculation which raised some degree of reasonable apprehension in the man s mind for the prospect on his wedding night

Difficulty in penetrating or in fitting a sheath may be an unexpected cause of premature ejaculation but the truth is that most men ejaculate very quickly when they first make a satisfactory penetration It is their reaction to this experience which determines whether or not they are to become premature ejaculators

The fortunate ones are those who find pleasure in the experience brief though it is they are eager to repeat intercourse, which they do until ejaculation is sufficiently delayed for their full satisfaction Since in the normal young man the capacity for erection always outlasts that for ejaculation this cannot fail to happen Experience stabilises the reflex, and though ejaculation will always occur more quickly after a period of abstinence, this does not constitute prematurity To those who ask how long should it last? the answer is as long as you want it to

The unfortunates are those who are abashed and lose their erection or decide that it is wiser to postpone a second attempt until the next day when inevitably the same thing happens So they delay again hoping that the trouble will settle down or that in time they will discover a successful method of restraint

If one of these men consults his doctor he will probably escape with a dose of phenobarbitone too small to impair his potency and an assurance that the trouble will improve in time His lot is easier than that of the man who reads marriage manuals and still further distorts the natural pattern of his intercourse by attempting techniques of restraint. Both are infinitely better off than the man who sees a psychiatrist and learns that his incompetence is the symptom of some hidden defect in his emotional life

Some of these men have such robust sex drives and such sturdy constitutions psychologically that their sex life persists for many years They derive little pleasure from it but they carry on to please their wives or out of a sense of self respect accepting their disability philosophically More usually though the intervals between attempts at intercourse gradually lengthen and erections fail early as is only to be expected of any activity which does not receive its physiological reward

These patients often complain that they are too tired for intercourse or feel exhausted after it The fact that normal men do not make these complaints has led some people to suppose that the tiredness is psychological It is on the contrary quite natural because such patient, to have intercourse, must make a great effort of restraint during the act, and find courage to face the disappointment and often his wife's exasperated tears when it is over

*Treatment*

Treatment seems too grand a word for telling a man to abandon all restraint and have more frequent intercourse, but that is all that is required Of 60 uncomplicated cases under 40 years of age, 51 reported that they were making satisfactory progress after a single visit and needed no further help, 5 were seen twice, and 4 between three and six times before the same result was achieved Difficulty in getting sufficient erection sometimes arises in older men and in long-established cases and this must be dealt with on the lines already described

Some men cling to the popular idea fostered by marriage manuals that a man can, or should, control the moment of his ejaculation This error must be responsible for a vast amount of suboptimal sexual function, for, while there are excellent reasons for planned control of sexual opportunities both restrictive and expansive according to circumstances, nothing is ever gained by detracting from the spontaneity of the sexual act itself There is in fact no way of delaying an orgasm during intercourse, and, if the claims of those who say they can do so are examined, it will be found either that they cease all movements or so much restrain them, that in effect they stop intercourse, or else that they are living so well up to their sexual capacity that they cannot ejaculate unless they make a special effort to do so The ideal of a simultaneous orgasm in the man and woman is usually achieved when the man himself needs the additional stimulus of the woman's orgasm to bring on his own

Not uncommonly a man reports after a few weeks that he himself is all right but that his wife is still without an orgasm Seeing that many women take several months to reach orgasm, even when married to a competent male, it is only to be expected that one who has been deconditioned by a husband with premature ejaculation should take much longer I always make this clear to couples and advise the husband to ignore his wife's reaction, for a woman's orgasm is like a man's erection—an involuntary reflex—and the more she strives the less likely is she to achieve it Above all, a husband should never ask If he is in doubt, the answer is "No," and asking only adds to the wife's difficulty by making it appear that their intercourse has been a failure Any woman's capacity for orgasm on one particular occasion is unpredictable Woman's orgasm depends more on the natural, unrestrained rhythm of intercourse than on the number of minutes penetration can be sustained without ejaculation For a man to attempt restraint is equivalent to trying to drive his car at full speed with the brakes on Men, like motorcars, do not last long under such treatment

Patients' replies to follow up letters show that the result is usually a gradual improvement, and the lack of a clearly defined end point may explain the failure of such a high proportion to report their progress The improvement, however, influences their whole relationship, and at least in their opinion, it has been related to the advice they were given rather than any "psychological" influences Thus a man who had been married two years said six months after his only visit "It's made my married life, it's like getting married again, we don't get on each other's nerves and we're more contented", and another "the treatment prescribed has been doing me a lot of good and I think I need not another appointment" As only half an hour is for the initial consultation, it would hardly be le to exert much psychological effect

## Absence of Ejaculation

Any man may on occasion fail to ejaculate beca short a period has elapsed since he last did so, or he is not getting enough stimulation from the activity in which he is engaged But a small prop of men (about 3% in this series) have never during masturbation or intercourse, though ther experienced nocturnal emissions

If it were practicable to standardise cond measure the average time taken for ejaculation by a of men, and plot it against the numbers of men time period, the result would no doubt be a curve resembling the curves obtained when the d tion of any other variable natural quality, such as or intelligence, is similarly recorded The qualit measured in this case would be the natural exci of the spinal cord reflex are concerned

*Cause*

The most important factor in lowering the exci of this reflex is age Kinsey's observation that fr of orgasm declines before full maturity is reached s that reduced excitability rather than any def potency is the cause It is probably significant th average age at which the first attempt at took place was 32 years for this group as ag years in the other cases

All except 1 was physically and psychologicall they had good employment records and had adjustments in their marriages despite their The exception differed only in being a very s chistic fetishist who had married at 43 He co originally of erectile impotence but was fully coöp in treatment and became potent only to find eja was still beyond his reach

*Treatment*

One's scope for increasing excitation is limited advice on technique, including the employme fantasies, and the application of a vasodilator, s 'Trafuril,' to the penis may help Of the various cological remedies, I have found a proprietary containing amphetamine sulphate, strychnine, and yohimbine the most helpful in bringing near to orgasm, though never to success Oestr was ineffectual Testosterone revives erection increases sexual excitability generally and the of semen, but I have seen no direct success from

2 of the successful cases are reported below and 8), the 3rd only needed advice on techn 4th man is worth mentioning because he had alre successful by the time of his appointment

In terms of improved technique there was no exp He was 31 at the time of his marriage and first and for the first four months he succeeded in ex masochistic fantasies on which his sex life had form This left him with sufficient erection for pene checked ejaculation However, after making his a the fantasies broke through and he immediately A feeling of disquiet at their persistence was the his visit

## Results of Treatment

The following figures, based on a postal various intervals after treatment, give a gene the series, and the results, on which this based

| Disability | Did not reply or not treated | Failed | Satisf with impro men |
|---|---|---|---|
| Insufficient erection | 97 | 18 | 130 |
| Premature ejaculation | 96 | 2 | 107 |
| Absence of ejaculation | — | 6 | 6 |

## Illustrative Cases

ase 1 —A clergyman aged 32 had been married nine rs. As an undergraduate he took his work very seriously ried about philosophical problems, became depressed attempted suicide While still at the university he met -wife and passionate desires developed so they thought it ıt to get married; but being unable to support children y decided that their contacts should stop short of inter rse. This was not attempted until about eighteen months r marriage when he had difficulty in penetrating ejacu d prematurely and failed He was advised to have chological treatment, but this had no effect on his sexual acity

his man's history included a depressive episode and ral major inconsistencies. But his personality com ded respect and it was a far less serious matter to ask to make some temporary concessions toward sensual lgence than to probe his psyche if one had the pre ption to do so; or to question the guilts and anxieties h must anyhow afflict a young man of his temperament unately his wife was one who could manage the para ical situation of stimulating his desire without appearing sk anything for herself He was given the usual advice an implant of 100 mg testosterone and two months was successful after six visits. He wrote eighteen months to say that they had a baby and everything was factory

ase 2 —This man, aged 28 had been married two years ıad completed a pilot's training but the war ended before ad flown many hours. On demobilisation he went on the o and worked hard in repertory companies; but seeing uture for himself had found an opening in business, and due to start in a month. He had a lively responsive onality and was active and intelligent. He had no guilt it masturbation but on the half-dozen occasions he had intercourse before marriage (not with his wife) he had felt at ease and though he never failed he had not ed much pleasure. His wife had started menstruating heir wedding day and the strong erections with which d started began to fail before he could begin intercourse till had erections on waking and on contact with his wife hey failed every time before penetration His intelligence his temporary unemployment (without financial stress) him an ideal patient. If the method was right he must ed He was therefore told that if he did not write in days he would be sent a second appointment to come his wife As no letter came the appointment was sent e last minute Fortunately the residual disability was letter writing He wired immediately: Interview essary machine functioning delighted and grateful ng

se 3 —A bank official aged 38 had been married two and had a son a year old. As a boy he had masturbated three times a week, and later he had had involuntary ations on contact. When he had intercourse it never more than three or four thrusts Intercourse had occurred more than once a night since his marriage e felt so ashamed that for some time it had sunk to once th He wrote three weeks after his visit following your and my wife's visit to Dr L. (to whom I had referred contraceptive advice) there has been a marked improve in our sexual relationship We found the cap a benefit but no doubt the main advantage was a more stic outlook on the question

cord this case in fairness to any critic who maintains ny treatment is really psychological It is inevitable patients should experience feelings of optimism onfidence once they can see clearly a way out of grievous difficulty But as the bottle of medicine ses their evidence is not reliable

e 4 —A 16 stone docker (aged 28) of enormous strength en three years married and had a daughter of 18 months. a typical mesomorph with an amicable disposition and tioning self-confidence He had never consulted a nor would he have done now if his young wife had not ferred to a gynæcological department when her lack al satisfaction was discovered He himself did not his sexual history was a proper subject for inquiry but ured that puberty was early and that street-corner intercourse started at 15 He regretted that his wife had no enthusiasm for intercourse but did not suspect that there was anything wrong with him. Were you too quick? Dunno 'How many thrusts? About three or four

He came back in four weeks. At first he had had intercourse as many as four times in succession; it lasted ten minutes and his wife had had several orgasms Though inarticulate he was very grateful

Case 5 —A wood machinist aged 23 had been married for eighteen months. His case is included because it illustrates the universal neglect of proper inquiry into sexual function and the way in which failures from other branches of medicine are accepted for treatment by psychiatrists

His trouble was pruritus ani which started a few weeks before his marriage Despite thorough dermatological treatment it persisted and he was accepted by a psychiatrist and passed to me for treatment The psychiatric notes gave no indication of the probable trouble but said that he was emotionally unstable and rather tense Sexual function was noted as being normal though the patient said that he had mentioned that he always reached orgasm before his wife and had been advised to restrain himself

The sex history was typical. Puberty early; a strong urge to masturbation, sometimes gratified twice daily despite guilt He had been physically interested in women since he was nineteen, and was liable to involuntary ejaculation on clothed contact He had married after demobilisation and had had intercourse three times a week since He felt this was the most that he could safely indulge in yet despite the maximum restraint he rarely reached a dozen thrusts before ejaculating

He accepted my usual advice and three weeks later reported that he had had intercourse almost every night and that it now lasted the full time" The irritation was very much less. By the end of six weeks he had settled down to five nights a week the itch had disappeared and only faint traces remained in the skin. He and his wife felt fully satisfied

Case 6.—This was a successful professional man of 35 he had married at 30 and had a son 2 years old He was very hard working sensitive and most considerate of his wife.

Puberty was at 13 and soon afterwards his father told him ' all about things and said it was a bad thing He never masturbated He first had intercourse at 21 He was always quick the first time but usually had two or three ejaculations at a time and both partners were satisfied until his wife became pregnant Intercourse ceased early in pregnancy owing to threat of miscarriage and when it was resumed four months after the birth of the baby he was very quick. His wife then had little desire and was upset by his premature attempts Twice when they were first married her cervical cap had been extracted with difficulty by a doctor so they would not use it He found sheaths troublesome He developed a gastric ulcer and was in bed for six weeks and his wife had been " under the doctor ever since her confinement.

He came again six weeks after his first visit but was no better The contraceptive trouble had been settled but his wife had no enthusiasm and he felt that her health forbade repeated intercourse while her lack of welcome damped his ardour

This common vicious circle infrequent intercourse—premature ejaculation—lack of satisfaction—diminution of desire—infrequent intercourse can be quite troublesome to break but eight months later he replied to a follow-up letter: The relationship between my wife and I has improved immensely "

Case 7 —An accountant aged 28 had been married three years Puberty was at 12 and he had had regular physical contacts with good erections and enjoyable sensations since adolescence He had regular intercourse for the first two years of his marriage but he never ejaculated except during sleep He had several months psychological treatment without avail and was given a hopeless prognosis by a recognised authority His wife badly wanted a child and gave full range to her disappointment in tears tantrums, and reproaches. When he was first seen his erections were poor and in intercourse rarely occurred. An implant of 150 restored his erections and gained a spell of his wife but despite every effort the orgasm him. He noticed however that nocturnal followed attempts, so he was given a Malleson artificial insemination syringe and advised the days on which conception was most probable Sexual activity was kept going for six months in the hopes of achieving a pregnancy in this way with little expectation of any other result

Then, one evening whilst watching television (he said bored not stimulated by it) he had the desire for intercourse and it took place in the sitting room (I think this is significant as illustrating the importance of spontaneity to both partners ) His wife was more than usually responsive, their movements rapid and synchronous, and he ejaculated He has continued to do so ever since and his wife is now pregnant and contented

**Case 8**—A Civil Servant, aged 28, had only been married five weeks He had a generalised ichthyosis and had suffered from a prolapsed disc Since the age of 16 he had had physical contacts with erections but had never attempted intercourse before marriage or had any ejaculation except in sleep His main complaint was absence of ejaculation, but he had a lot to say about his lack of agreeable sensations

Never having succeeded with one of these cases at that time, I did not welcome him and can only remember that I chided him for his superficial approach Not until I was going through the records seven months later did I notice that he had cancelled his second appointment ten days after his visit, with a letter to the clinic thanking me for "sympathetic and helpful counsel" Thereupon I wrote asking what advice I had given him and in what way it had been helpful, to which he replied

> 'I have indeed overcome my little trouble thanks to your help You may remember that I had no difficulty in achieving erection but I came to you with the question What is the point ? I thought I was supposed to enjoy it' On your advice I forgot about enjoyment and set out merely to find what pleased my wife This resulted in my performing the normal movements of intercourse without taking any interest in it at all, but I found that she responded at once It all ended in an ejaculation which seemed to last only a second or two and although enjoyable didn't seem to me to justify the effort However there was a starting point and using my wife's reactions as a guide to speed I performed this artificial process fairly regularly It was a case of pleasure by proxy because my main enjoyment came from a sense of power as I found myself able to give pleasure
>
> "As you said I would, I have gradually acquired a taste for this business and now I enjoy it from beginning to end"

**Case 9**—Sexual fantasies based on immature girls had worried a solicitor aged 32 since adolescence He had never indulged in any contact or, even in imagination, wanted intercourse He married at 28 without any previous sexual experience, but intercourse was precarious from the start and he tried to halt its decline by getting his wife to substantiate his fantasies in speech and dress This was not successful, he became completely impotent and failed in two jobs. His wife had just left him and started proceedings for mental cruelty

He was told that his fantasies were probably shared by a fair number of pubertal boys and later abandoned as opportunities for contact with older girls came along It was his misfortune that a shy, sensitive nature and careful upbringing had denied him these opportunities His mistake was trying to exclude the fantasies and then later to enact them He should have taken them to bed with him and in time they would have receded

Notwithstanding that he saw his wife the next day and allowed her to get the gist of my advice from him (receiving in exchange some blistering comments on my depravity), she returned home Intercourse restarted and they both experienced greater satisfaction than ever before He said that apart from the recovery of his potency he felt a completely new man so great was the load now off his mind

Was he right ? Or is he still a psychological mess whom I should have left impotent so that I could have pulled his psyche to bits and rebuilt it ?

## Conclusion

There seem to be only two possible primary causes for sexual impotence The first and generally accepted view is that it is psychological, the result of faulty personal relationships, and that therefore the first object of treatment must be to unravel and readjust these The alternative view which I have tried to put forward is that the primary cause is a faulty development of the [illegible] reflexes, due fundamentally to the restraints of [illegible] Naturally these restraints react on the more sensitive men, and inevitably, once impote established, secondary stresses arise between and wife These stresses may take up so much picture that they appear to be the primary ca may sometimes be that the resolution of these allows the natural force of recovery to succeed

I suggest that psychological investigation is indicated until one is satisfied that physiological re ments are fulfilled It has been my experience th this is done nothing more is needed

It would be wrong for anybody to conclude just because social restraints sometimes cause in susceptible men these restraints should be For one thing there is no way of knowing wheth not impotence is a serious problem in the populat large, and for another there is still much to be l about the effect on society in general of such Better sex education within the existing limits probably have prevented all the cases I have but it would have to be on different lines from th any of the existing marriage manuals

The writings of Gesell, Sheldon, and Kinsey prov background for this work But for the force that swimming against the tide for five years without ad I am indebted to the rigorous training, in making an on my own observations, which I received fifteen yea Charing Cross Hospital from a neurologist to whom I very grateful

# TORSION OF A FALLOPIAN TUB

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TORSION of a fallopian tube is rare and is sel ever, diagnosed preoperatively, because it prod pathognomonic symptoms or signs This is es true when the tube is known to have been in the case reported here

The first case was published by Bland Sutton (18 Régad (1933), reviewing 201 cases of torsion, fou in 24% *the tube had previously been apparently* heal 18% *it was a hydrosalpinx*, in 14% it was part of a in 13 5% there was infection, tumour, or ectopic, and in 12% there was an intra uterine pregnancy

Torsion during pregnancy was fully reviewed by (1936), who gathered 13 previously published cases an 1 of his own, and Caldwell (1949) and Kushner and baum (1952) have since reported similar cases Mu (1948) described a case of torsion of a previously healt in a non-pregnant woman

Reviewing the ætiology and mechanism of torsion, Blum and Sayre (1937) discussed many and examined the influence of anatomical malform peristalsis of uterus and tubes, venous engorgeme sudden body movements in initiating torsion presence of disease

The predominating clinical feature is sudden pain in an iliac fossa, associated with localised and tenderness and usually nausea and vomitin temperature is usually normal Tachycardia present Uterine bleeding, which follows the pain, is presumably due to pelvic congestion T be compared with the absence of bleeding shortl torsion of the pedicle of an ovarian cyst Sy referable to the *urinary tract* (McKerrow 1934) or alimentary tract have been observed The severit symptoms depends on the degree of torsion, the of interference to the blood-supply, the extent of (Anderson 1945), involvement, if any, of the and the extent of venous thrombosis

The similarity of the symptoms to those of pregnancy, a small twisted ovarian cyst, salp dicitis mesenteric lymphadenitis and strangulated make accurate preoperative diagnosis difficult cases collected by Savage (1936) and his own case nisdiagnosed A helpful diagnostic feature is the ce of intraperitoneal serosanguineous fluid com le with that found in early cases of ectopic gestation be found by aspiration of the pouch of Douglas

## Case report

arried woman aged 32 who had borne one child was en and admitted to the Jessop Hospital for Women ld, on June 8 1954 with the history that on June 6 d a sudden attack of colicky intermittent pain in the ac fossa and radiating to her back and down the lateral of her left thigh. She felt nauseated and vomited The pain was followed shortly afterwards by vaginal ng, but the loss did not cause any worry because this bout the time of her expected menstrual period She l that menstruation had always been regular 5 28 at the last monthly period which had been quite normal n May 11—28 days before admission

*examination* she was pale with pulse rate 100 normal rature and blood pressure 120/75 mm. Hg Her en was slightly distended rigid and tender in the left quadrant there was no evidence of shifting dullness ination per vaginam showed a normal anteverted mobile s and normal right tube and ovary There was, however tenderness on movement of the cervix and a tense r mobile swelling as big as a plum was palpable to the of the uterus. Either ectopic gestation or a twisted an cyst was provisionally diagnosed though the signs ymptoms were not altogether typical of either condition on of the tube was not considered.

*ration* —Under general anæsthesia the above mentioned gs per vaginam were confirmed and on aspiration e pouch of Douglas some faintly bloodstained serous with crenated red cells was obtained At laparotomy the neal cavity contained about 8–10 oz. of fluid similar at removed by aspiration. The uterus and right adnexa ared normal (the right ovary contained a recent corpus m) The left fallopian tube however had undergone ckwise twist of 540° and was distended with blood The vary appeared healthy apart from some exudate on its e The left tube was removed

*stoperatively* recovery was uneventful and the patient discharged on June 22 Seen on July 20 she was in good *h and said she had menstruated normally on July 14*

*hology* —The specimen removed at operation was a ian tube whose proximal part appeared normal and part dilated to 1 inch in diameter The fimbriated end bliterated by partially organised clot Section of the d part revealed blood-clot in the lumen and hæmorrhage wall Histologically apart from the extravasated blood artial tissue necrosis, there was no evidence of pregnancy ere any chorionic villi seen in the clot The condition hat of hæmatosalpinx due to torsion in an apparently y fallopian tube

## Discussion

is case is a typical example of hæmatosalpinx o torsion of a healthy fallopian tube The chief s of interest are as follows

The cause of torsion as in most of these cases, is wn but pelvic congestion brought about by the approach enstrual period may have been a factor

The original diagnosis was erroneous.

Uterine bleeding following on the torsion was probably secondary vascular engorgement a common finding o gynæcological complications.

Although aspiration of the pouch of Douglas did not lish the diagnosis it was of real assistance in the decision arotomy

*Conservation of the ovary on the affected side was* le even though the tube had undergone a twist of 510

## Summary

ase is reported in which torsion occurred in a usly healthy fallopian tube

In many cases the cause of the torsion is unknown but pelvic disease appears to predispose to this accident

Torsion of a fallopian tube can seldom if ever be diagnosed before operation, but symptoms and signs similar to those of torsion of a small ovarian cyst with the addition of immediate uterine bleeding should bring the possibility to mind

Aspiration of the pouch of Douglas should produce evidence similar to that found in early ectopic pregnancy

The decision regarding whether the ovary can be conserved or not must necessarily be made at laparotomy

I should like to thank Prof C S Russell for his permission to publish this case and for his helpful criticism and advice

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# TORSION OF THE TESTICLE

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THE clinical picture of torsion of the testicle is characteristic and descriptions of it vary very little Aird's (1940) account is representative There is sudden pain nausea vomiting swelling of the testis and usually an effusion in the tunica vaginalis The agonising pain particularly impressed Lambert and Smith (1938) when they surveyed cases in boys at Rugby School and Walton (1952) states that pain redness swelling, and œdema are always present in such cases

The following case is of interest because it showed not one of these features

## Case report.

A man aged 23 was admitted to Chase Farm Hospital on Aug 31 1954 with six days history of a slightly tender swelling in the right inguino scrotal region He had had a little pain scarcely more than discomfort, in the swelling and in the lower abdomen but it had not been severe enough to keep him away from work He had not had nausea or vomiting and his bowels had been open regularly The day before admission he had experienced some discomfort on walking and consulted his doctor who diagnosed an inguinal hernia in danger of strangulation and sent him to hospital The symptoms had abated in the twelve hours since he had seen his doctor There had been no inguinal swelling and the testes had both been in the scrotum before the onset of this episode He had neither strained himself nor injured his scrotum

*Examination* —He was thin and pale a poor witness and of low intelligence He was quite comfortable with a clean moist tongue and a temperature of 97 8°F and pulse rate 88 On the right side there was a tense and slightly tender mass measuring about 3 inches by 2 inches, in the inguino scrotal region. The overlying skin was normal in colour and temperature The mass did not allow transillumination and there was no impulse on coughing The testicle could not be felt separately from the swelling and the scrotum hung considerably lower on the right than the left Sensation in the left testicle was normal There was no abdominal tenderness or swelling and rectal examination revealed only soft fæces Normal bowel sounds were present An obstructed inguinal hernia was diagnosed The possibility of testicular torsion occurred to the admitting officer who rejected the diagnosis because he had had the condition and he feelingly contrasted his own agonising sensations complete comfort of the patient before him

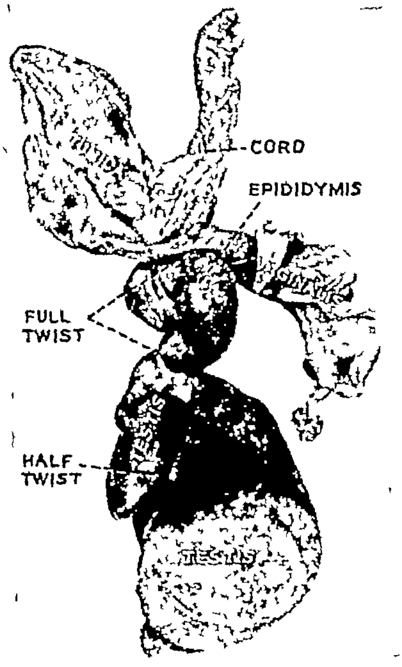
*Operation* —About six hours after admission local anæsthesia was induced with $1/2$% lignocaine, and a right oblique inguinal incision was made The inguinal canal contained only a slightly œdematous cord, and the swelling consisted of a purple testicle and epididymis in the tunica vaginalis The mass was delivered out of the scrotum, and the tunica was opened A few ml of fluid escaped The body of the testicle was twisted on itself through a half turn There were further complete twists between testicle and epididymis and at the proximal pole of the epididymis The whole testicle and epididymis were gangrenous Orchidectomy was performed, and the incision was closed A small drain was left in the scrotum and removed after forty-eight hours

*Postoperatively* progress was uncomplicated, and the patient was discharged on the eighth day with his wound completely healed The Wassermann reaction was negative

## Comments

It is not uncommon for a maldescended testicle which has undergone torsion to be diagnosed as a strangulated inguinal hernia, but this testis, according to the patient, was fully descended Epididymo orchitis is the more common misdiagnosis of the lesion when the testis is normally placed, but this patient had little swelling, no redness, no pyrexia, and only slight tenderness

Hamilton Bailey (1936) says that torsion cannot take place in a normal testis Complete and high investment of the testis and epididymis by the tunica vaginalis enables the testicle to rotate freely within its enclosing sac Such a high investment was present and can be seen in the accompanying figure, but it is difficult to understand how this could have influenced the twist in the body of the testis and that between the testis and the epididymis



**Operation specimen The parts were identified histologically (Two-thirds of actual size.)**

It has been said that a scrotal abnormality is likely to be bilateral, and after torsion has taken place on one side it is wise to fix the contralateral testicle Ewert and Hoffman (1944), however, found that bilateral torsion had taken place in only 26 of the 489 published cases they were able to collect It therefore seems justifiable to keep this patient under observation and to operate only if symptoms arise It is essential that he should report to his doctor and be sent to hospital immediately if any scrotal discomfort or swelling develops

Thanks are due to Mr Max Pemberton, under whom the patient was admitted, for permission to publish

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# TORSION OF THE OMENTUM

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CASES of omental torsion are rare enough, following 4 came under my care in the short eight weeks, and all of them were associated œdema of the peritoneum and abdominal muscles, complication I cannot find reported anywhere

## Case-reports

**Case 1** —A man, aged 31, was admitted on March with twenty four hours' history of pain in the fossa, unaccompanied by nausea and vomiting, and hours history of diarrhœa

*On examination* his pulse rate was 68, respirations temperature 98°F His tongue was clean, and there fœtor oris His abdomen was soft and moved on and bowel sounds were heard His right iliac fossa resisted pressure, and showed rebound tenderness examination was negative

*Operation* —The abdomen was opened through a incision, and the oblique muscles were found to be and the peritoneum thickened When the perito incised, bloodstained fluid welled up The normal, but the greater omentum was swollen, thickened down the lower three quarters of its right which had rotated clockwise, but the number of not be assessed No cause for the rotation The affected portion of omentum was resected abdomen closed The patient's postoperative reco uneventful

**Case 2** —An obese retired sea captain, aged 73, ted on March 15 to Burnham on Sea Hospital with hours' history of lower abdominal pain He had once, and the pain was greatest in the right iliac over the right external abdominal ring

*On examination* his pulse rate was 80, respirations temperature 98°F His tongue was clean, and there fœtor oris His abdomen moved normally, but exquisitely tender at the outer border of the right abdominis muscle, where an indefinite mobile be felt

*Operation* —A right paramedian incision was made an œdematous abdominal wall When the peritone opened, a large quantity of bloodstained fluid and the mass was obviously greater omentum abnormality was found in the abdomen, and there adhesions of the greater omentum either to abdomina contents and no herniæ The lower border of the omentum was almost gangrenous and twisted clock times on its long axis The affected portion was by serial ligation proximally and resection The recovery was uneventful.

**Case 3** —A male clerk, aged 22, was admitted with five days' history of pain to the right of his This had persisted up to the time of his admiss it had moved to his right iliac fossa and become had had nausea but no vomiting Slight diar been present on the third day He had bee weight

*On examination* his pulse rate was 98, respiratio temperature 98 6°F His tongue was clean, and no fœtor oris His abdomen moved normally on and bowel sounds were heard The right iliac fo tender and resisted palpation Rectal e negative

*Operation* —Laparotomy was done through a incision, and the oblique muscles were found to be and the peritoneum much thickened Bloo was present in the abdominal cavity The normal, but a thickening was felt higher up, to be in the greater omentum, which had a thick coloured right border which had rotated clock affected portion was ligated and resected, and closed. The patient's convalescence was unevent ase 4.—A girl aged $5\frac{1}{2}$ years, was admitted on May 11 [illegible] five days history of stomach ache followed by pallor [illegible] pain became acute just before admission and was [illegible] ralised over the abdomen. There was no vomiting but [illegible] sea was present. The bowels had acted regularly and [illegible] had been no urinary symptoms

[illegible] *n examination* her pulse rate was 120 respirations 25 temperature 100°F There were no signs in her chest or [illegible] ral nervous system. Her abdomen moved normally on [illegible] ration but there was much tenderness with guarding in [illegible] right iliac fossa. Rectal examination revealed hard [illegible] but no tenderness

*[illegible] peration*.—My house-surgeon (Dr M Ree) *opened* the [illegible] omen through a McBurney's incision and noticed that the [illegible] oneum was thick and œdematous. The abdomen con[illegible] d sanguineous fluid and the greater omentum was black [illegible] thickened down its right border which was twisted [illegible] cwise A few rubbery glands were present but otherwise [illegible] ing abnormal was found The twisted omentum was [illegible] ted the appendix removed and the abdomen closed [illegible] patient's postoperative recovery was rapid

### Summary

[illegible] cases of omental torsion occurred in eight weeks [illegible] men and 1 in a girl. The youngest patient was [illegible] years (I have not heard of this condition at so [illegible] an age) and the oldest 73

[illegible] cases were of the primary (Payr's hæmodynamic [illegible] on) type all affecting the right free border of the [illegible] ntum The 4th (case 2) was a lesion of the lower [illegible] er of the greater omentum In all the rotation was [illegible] kwise.

[illegible] l 4 cases presented signs suggesting appendicitis but [illegible] was no furring of the tongue or fœtor of the breath, [illegible] except in case 4 there was neither pyrexia nor rise [illegible] ulse rate.

[illegible] ne feature common to all which I cannot find [illegible] tioned in any published report, was œdema of the [illegible] minal muscles and peritoneum The presence of [illegible] former tempted one to make a diagnosis before the [illegible] toneum was opened

[illegible] no case was an obvious cause for the torsion found

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## Preliminary Communication

### IE EXCRETION OF PHOSPHOETHANOLAMINE AND HYPOPHOSPHATASIA

[illegible] E have during the past year been studying some [illegible] of infantile and adult hypophosphatasia In [illegible] tion to the changes in the bones and tissues that [illegible] been noted by others we have made an observation [illegible] has not so far been reported As increasing attention [illegible] ing paid to hypophosphatasia by physicians and [illegible] iatricians we have decided to report our observation [illegible] y so that others interested in this aspect of the [illegible] se may study it on their own cases.

[illegible] ine obtained from a two month-old male child [illegible] ing from hypophosphatasia and which showed the [illegible] rachitic bone changes hypercalcæmia and a [illegible] lkaline phosphatase in the serum was subjected to [illegible] partition chromatography for amino acids. A [illegible] orresponding to that for phosphoethanolamine was [illegible] No corresponding spot for ethanolamine was [illegible]

[illegible] phosphoethanolamine can act as a substrate *for the* [illegible] ne phosphatase, the excretion of this *substance* [illegible] ine of these patients appears to us to *be of* [illegible] and to indicate one way in which their [illegible] be deranged

Medical Research Council
[illegible] ment of Experimental Medicine
University of Cambridge

University College
Hospital Medical School

R A Mc[illegible]
M.D Ca[illegible]
A. B [illegible]
M B [illegible]
[illegible]
[illegible]

## Medical Societies

### ROYAL SOCIETY OF MEDICINE

### The Future of Neurology

A MEETING of the section of neurology was held on Jan 6, with Prof F J NATTRASS the president, in the chair

Sir FRANCIS WALSHE F R.S made a plea for a more realistic approach in neurological research The primary responsibility of neurologists, he said, was to seek the cause of illnesses and find ways of curing and preventing them could it truthfully be claimed that present research was directed effectively to this end ? Nobody disputed the value of the contributions made by the neuro anatomists and neurophysiologists but, despite a century of nosography and morbid anatomy, the cause of disseminated sclerosis motor neurone disease and the metabolic disorders of the nervous system remained undetermined and we were as far as ever from finding a cure for them

The fruitful investigations of the pioneer physiologists had led later workers to assume that study of the anatomy and physiology of the nervous system would inevitably yield an answer to every ætiological and therapeutic problem. This belief persisted even today, as was shown by the eagerness with which the younger generation of neurologists had seized upon the new diagnostic electronic devices Yet it had to be conceded that in the last twenty years all major advances in treatment had resulted from chemical studies—studies made moreover, not by clinical or experimental neurologists but by workers concerned only incidentally with nervous diseases. Thus though the symptom-complex of subacute combined degeneration of the cord was identified in 1900, not until twenty-six years later did workers—outside neurology—determine [illegible] ætiology and provide the effective remedy ; and many similar instances could be cited

"All around us in medicine," said Sir Francis, "[illegible] find physicians working in chemistry and biochem[illegible] or in any discipline that may be needed to elu[illegible] the medical problems upon which they are eng[illegible] and it was nothing less than [illegible] and lack of vision that had prevented [illegible] from [illegible] same To regard n[illegible] as concerned [illegible] mainly with what could be seen in a micr[illegible] post mortem room was [illegible] this time to ta[illegible] and obsolete view

Welcoming the Medical Research C[illegible] creation of [illegible] to enable young [illegible] train for three [illegible] relevant sci[illegible] Sir Francis said [illegible] was an ex[illegible] of admi[illegible] which [illegible] needed. [illegible] was [illegible] neurolog[illegible] of the Royal [illegible] who [illegible] defined [illegible] training [illegible] the basic [illegible] some time work[illegible] possibility [illegible] Sir Franci[illegible] was to [illegible] and was [illegible] [illegible] PATLING [illegible] to [illegible] The [illegible] extent to which it assimilated contemporary discoveries in the laboratory, and on its ability to induce scientists to undertake the investigations likely to prove most profitable to practical medicine A great present need was for the re establishment of close and productive relationships between medical men and scientists

In the advance of medical knowledge there had been little in the way of any organised attempt to distinguish between major and minor objectives, or to estimate the adequacy of the available resources For instance, how many investigators were engaged in unravelling the pathogenesis and chemistry of the demyelinating diseases, which all agreed were fundamental problems in neurology? The failure to assess the relative importance of the many problems which confronted us was one of the most serious deficiencies of modern medicine As a result, the none too large resources of medical and scientific investigation were being dissipated over matters of lesser consequence

Referring to neurophysiology, Professor Payling Wright asked whether there was justification for letting the study of the biophysics of neurones absorb so much of the resources of neurology Attention might be paid more profitably, he believed, to the vessels of the central nervous system and to the cells of the neuroglia, and he urged that younger investigators be encouraged to inquire into the obscurity that still envelops the reactions of the nervous system to drugs and allergens, as well as into the biophysics and biochemistry of its tissue fluids Biochemistry, in particular, seemed to him the discipline most likely to infuse neurology with new and productive ideas, though the peculiar difficulties associated with the biochemistry of nervous tissues admittedly acted as a deterrent to workers in this field However, the introduction into biochemistry of the physically recognisable isotopes had provided medicine with an exceptionally powerful technique for exploring metabolic processes As a result, investigations could now be resumed into the hitherto baffling problems of the synthesis and breakdown of brain lipids—a field that had remained almost untouched since Thudichum and his followers had been forced, through exhaustion of their technical resources, to relinquish their pioneer studies

The future of neurology, Professor Payling Wright concluded, lay not in the isolation of problems and investigators but in the closer intellectual collaboration between those who saw and appreciated the important problems and those who could bring expert knowledge to bear on their solution

In the discussion that followed, Dr W **Ritchie Russell** drew attention to the serious shortage of neurologists throughout the country, and particularly in London He thought that, since the best facilities and opportunities for research were to be found in the universities rather than at Queen Square, what was needed was first to build up these university centres

Mr D W C **Northfield** pointed out that under the National Health Service little or no provision had been made to enable neurologists—or, indeed, specialists in any branch of medicine—to combine routine clinical duties with research He proposed that influence should be brought to bear upon those who arrange the National Health Service to make this financially possible

Referring to neurosurgery as the "naughty child" of neurology Mr **Wylie McKissock** said that the tables had lately been turned and it was the neurosurgeons who were now "repressing" the neurologists This policy was far from wise for neurology to advance, it needed to go hand in hand with all its associated branches, [illegible] ing the basic scientific disciplines He strongly [illegible] ted that a neurologist should always be appointed [illegible] r a neurosurgical team was established Dr [illegible] **Williams** agreed that the greatest benefits to neurology would result from workers in various rel departments of medicine collaborating in teams, he thought that new discoveries would have to c first from the fields of chemistry and physics before t could be much progress in neurology He remind audience that three biochemists supported by the Me Research Council were now working at Queen Squar

Summing up, Sir **Francis Walshe** reiterated his c tion that a fruitful future for neurology lay rather experimental pathology than with electrophysiol studies In the case of the latter it seemed that studies revealed more about the properties of the tus used than of the functions of the nervous sy

## Reviews of Books

### Prefrontal Leucotomy and Related Operations

*Anatomical Aspects of Success and Failure* A **Meyer**, M D Bonn, professor of neuropathology, I tute of Psychiatry, Maudsley Hospital, Lond **Elizabeth Beck**, research assistant, Institute of Ps atry, Maudsley Hospital, London Edinburgh & Boyd for the William Ramsay Henderson 1954 Pp 60 10*s* 6*d*

Based upon the William Ramsay Henderson le delivered by Professor Meyer in Edinburgh in 1 this book surveys anatomical investigations carried at the Maudsley Hospital on brains of leucotom patients who survived the operation long enough the result of the treatment to be judged. It is on 102 cases, of which 62 were histologically investigated—the largest group hitherto collected handling of this material was masterly, the planni the pathological procedure admirable, the investi systematic and painstaking, and the inte careful Since the patients were examined and in many hospitals and observed by various people different standards, conclusions could only be dr with caution Still, it was possible to give some an to one of the most controversial problems—namely, h much the clinical result was influenced by the quan of frontal lobe isolated, and how much it depended the locality of the operation There was consider more frontal-lobe interference

> "in the 24 much improved or recovered cases, as comp with the unimproved group This, of course, does not that the more of the frontal lobe is cut the better will be results, but it does mean that the cut must be adequ order to be effective While the quantitative factor retains its importance, a few facts have emerged which to some regional localisation The dorsal and, in part the dorsolateral sectors of white matter do not appear as significant for improvement as the mid central, and cingulate sectors On the other hand involvem the dorsolateral and lateral white matter, and partic cortex, appears to be one of the factors responsible personality change"

In correlating anatomical and clinical data the au come to the conclusion that cutting of the medial sector of fibres gives the best results in leucotomy also that the quantity of fibres removed in this seems to be important By studying the r degeneration in cells and fibres, they clarified ana problems which have hitherto been controversial, instance, they established that the magnocellular p of the dorsomedial nucleus and the anterior nucl the thalamus project into the medial orbital region that these nuclei receive fibres from the hypoth The granular prefrontal cortex sends fibres to the d medial nucleus of the thalamus only, and also a contingent to the hypothalamus and the pontine n Most of the efferent fibres originate from the agra cortex and end in the ventrolateral nucleus of the mus, corpus striatum, hypothalamus, red nucleus pons Fibres originating in the premotor parts of orbital region *and* in *premotor area* 6 end in v nuclei of the hypothalamus, the ventromedial nu of the hypothalamus seems to be the most impo end-station Schematic drawings illustrate the co cal connections, and an appendix tables the entire terial with the relevant clinical and anatomical he book presents well the basic anatomical facts to leucotomy

### Atlas of Epidemic Diseases

t II section I. Editor Dr Ernst Rodenwaldt delberg Sponsored by the Heidelberger Akademie Wissenschaften. Hamburg Falk. DM 57 50

ou the support of the Bureau of Medicine and of the U.S Navy has been discontinued, the volume of this work has begun to appear under nsorship of the Heidelberg Academy of Sciences go loose-leaf format is similar to that of the first [1] and the present section covers eight diseases— al dysentery in Africa; relapsing fever in Europe x in Europe rabies in Central Europe trachoma lm disease sleeping-sickness; and Chagas there is also a population map of the U.S.A The -the English version is still heavy going in places— more space than the maps but they remain no han notes. This gives a pointer to the major tual defect of the work Just as films are invaluable , but only as aids, in teaching, so maps—apart traight geographical maps—should be explanatory ts and not *pièces de résistance*

### es of the Skin

n ed. Oliver S Ormsby M.D., Rush professor of rmatology emeritus University of Illinois, and milton Montgomery M.D., M.S professor of derma ogy and syphilology University of Minnesota. London nry Kimpton 1954 Pp 1503 £8

ew edition of Ormsby and Montgomery is always ortant event. For many years this book has been the most authoritative works on dermatology in nglish language—an Osler of the dermatologists n it, the inquiring reader can find all the information eds, carefully tabulated and with comprehensive nces.

a moot point whether 1500 pages is not the limit of expansion; but in a work of reference such as this dliness is not such a disadvantage as in a textbook o in his senses would attempt to learn dermatology ding a work of this sort from cover to cover rmatological art can only be acquired by selective g in the light of clinical experience but even the experienced of dermatologists can advantageously o this book, overtly or secretly according to his hoping for guidance and often finding it when nted with a rarity or a difficult problem

ensive use in this edition has been made of other itative works on histopathology syphilology ogy, tropical diseases and the like and it also ns contributions by DeLamater Farber Kierland obitz. *Today multiple authorship is inevitable* n the whole desirable Dermatology is concerned so many aspects of life—social medicine, industrial ine toxicology psychiatry bacteriology, and cs—to mention only a few—that the days of rehensive monographic textbooks are passing

contents are as up to date as they can be in any large ok in this age of rapid progress. Amongst the recent ons are items on cat scratch disease incontinentia nti facial eosinophilic granuloma and self-healing liomata Ecthyma contagiosa may be the correct for orf as it occurs in sheep but is it appropriate to the o as it affects man? The section on tuberculosis con only a short reference to the use of isoniazid in lupus ris and states that it is ineffective in erythema induratum inion with which many would disagree There are many ent clinical illustrations both monochromatic and red There are also many clear photomicrographs with ptive matter on histopathology This is an ideal arrange helping the integration of clinical and pathological ht. This volume is, in fact two works in one a complete to clinical and histopathological dermatology

is sad to record that Dr Ormsby died last year the proofs of this book were being read This h edition is his monument and a worthy one

### Bedwetting

Portia Holman M.D. M.R.C.P. D.P.M London Delisle 1954 Pp 40 5s

A short clear, practical book on bedwetting is what every family doctor needs at some stage of his career and here it is From a large experience of children with this symptom Dr Holman is able to classify the types of case commonly seen to simplify diagnosis, and to assure the doctor who takes the trouble to differentiate between the types that there is a large group of bedwetters who will respond without consuming much of his time, to treatment which will put no undue tax on his skill.

### Liver Injury

*Transactions of the Twelfth Conference September 1953 Princeton N.J* Editor F W Hoffbauer, M.D associate professor of medicine University of Minnesota Hospitals. New York Josiah Macy jun. Foundation 1954 Pp 231 $4.25

The future policy of the Josiah Macy jun. Foundation is as stated by its medical director to restrict the conferences on any one subject to five. This volume is the twelfth and *last* of a series on liver injury, and a worthy companion to its predecessors The main subject was the rôle of the liver in the metabolism of the three major foodstuffs

Carbohydrate metabolism of the isolated perfused liver of rabbits and cats was discussed by Lundsgaard and a discussion followed on glycogen deposition in the placenta and the increased sensitivity of pregnant women to the diabetogenic action of corticotrophin and the adrenal corticoids In the section on fat metabolism, which dealt mainly with the rôle of co-enzyme A, Gurin presented the important results of his work on the synthesis of fatty acids from acetate by an in vitro system of water soluble enzymes extracted from pigeon or rat livers In the section on protein metabolism the emphasis rested on the effect of diet upon the composition of the liver cell and on the search for a suitable standard of reference for the quantitative studies.

### Prerequisites of Good Teaching

*And Other Essays* Dr Ernest Sachs, Research Associate Surgery and Medical History Yale University Hamden Connecticut: The Shoe String Press 1954 Pp 118 $2.50

In this humane and nicely printed little book, Dr Sachs presents some of his random thoughts as a teacher and practitioner of surgery In particular he has some interesting things to say about the value of well-chosen questions in the instruction of students. The hazards and responsibilities of our profession—such as the need to warn the family of the seriousness of a patient's condition or to comfort them when an operation has failed or the need to decide what to do when a case is diagnosed too late or whether to prolong life in a hopelessly ill patient—are considered wisely if not deeply and the generosity and integrity of the writer light up every page

### Physiology and Biochemistry of the Skin

Stephen Rothman M.D professor of dermatology University of Chicago Chicago University of Chicago Press. Cambridge: University Press. 1954 Pp 741 £7 0s 0d.

Dr Rothman's learned and comprehensive study of cutaneous physiology is a monumental work As cyto chemistry tissue-culture and the many other methods of studying the skin are likely to yield valuable results in the future this edition will probably be the first of several

The book begins by describing the mechanical properties of the skin and its electrical behaviour Other sections deal with absorption vascular reactions, sensory and secretory functions, heat regulation, the pH the lipid film keratinisation collagen and connective-tissue ground substance pigmentation, and hair growth. Obscure matters such as peroneal alopecia the higher iron-content of the hairs of red heads the differing pH of the skin of man and domestic animals, and many other fascinating subjects receive due attention Some of the photographs are excellent particularly those of nail fold capillaries catheterisation of apocrine glands cholinesterase in eccrine glands and cholinergic fibres experi mental miliaria, and club hair formation. The diagrams are all good

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[1] *Lancet* 1953 i, 628

The book contains something to help the inquiring mind on all dermatological problems and on the way in which Man responds to his environment It will be perhaps of most value to the physiologist and biochemist, but every practising doctor should find much in it to stimulate him, and after reading it he may feel competent to discuss the Krebs cycle as glibly as he (or his barber) already discusses the hair cycle , while sulphydril groups and disulphide linkages will seem like ABC

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**The Practice of Local Anæsthesia** (4th ed. London Sir Isaac Pitman 1954 Pp 275 25*s* ) —The purpose of this book is to give a relatively concise and practical picture of local anæsthesia to surgeons, general practitioners, and anæsthetists, studying for their diploma , and since it has reached its fourth edition Mr George Bankoff can fairly claim a good measure of success The first part deals with general principles, while the second and largest part gives a detailed account of the techniques for producing local analgesia throughout the body Unfortunately, though a thorough revision is mentioned in the preface, little reference is made to work later than 1940 This precludes any mention drug lignocaine, which for several years now has been lished in the forefront of local analgesics, and it may perhaps account for the author's outmoded view of anæstnesia

**Synopsis of Medicine** (10th ed Bristol John Wr Sons 1954 Pp 1253 35*s* ) —Sir Henry Tidy's mas of compression continues to summarise the facts of and instruct in common practices Probably not greatest poets can claim to be lifted so often or so from the shelves as " Tidy," and their advice is explicit

**Biology of Anopheles gambiæ Research in West Africa** (*World Health Organisation monograph no 9* M H. HOLSTEIN, Dr ès Sc Geneva World Organisation 1954 Pp 172 13*s* 6*d* ) —This is an edition of a useful monograph published two year French (see *Lancet*, 1952, ii, 1065) The text is sub the same, with the addition of one or two paragraphs to more recent work, and the bibliography has been from 388 to 410 references The translation is accur clear , but the English text seems to emphasise the liking for technical terms.

# New Inventions

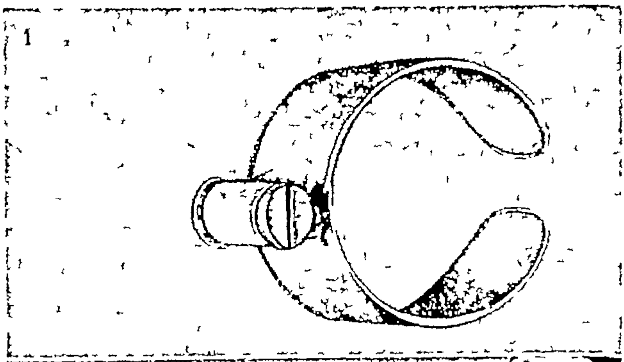
## VALVOTOMY KNIFE

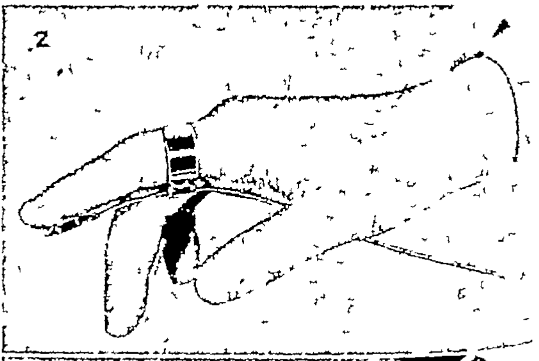
THE search for the ideal knife for mitral valvotomy still goes on Much time has been spent on attempts to solve this difficult problem It has always appeared to me that something quite simple would be the answer, and I suggest that Brock's knife, in its simplicity, is the most suitable instrument

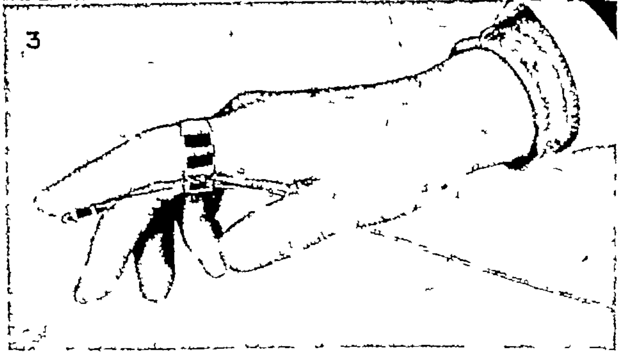
However, as the cutting edge of this knife is always facing the atrial and appendiceal walls, there is the great danger that during its insertion and removal damage might be inflicted Because of this danger I have developed a rotating mechanism (fig 1) to be used in conjunction with Brock's knife The cutting edge of the knife can be kept close against the finger during insertion (fig 2) and rotated into the cutting position (fig 3) the exact portion of the valve has been palpated anterolateral cut is then made When the knife has passed through 180° (fig 4), the posteromedial is cut with the same sawing action and without the hand On completion of these manœuvres the can be split further with the finger The knife and are then withdrawn with the cutting edge again finger A clamp can be applied to the appendage purse-string sutures can be tied slowly as the fing knife are withdrawn together

It is a pleasure to thank Mr J Hartwell, who m prototype The instrument can be obtained from M Chas F Thackray, of Park Street, Leeds, 1

M LENTIN
Bolton Lancs M B N U I., F.R.C







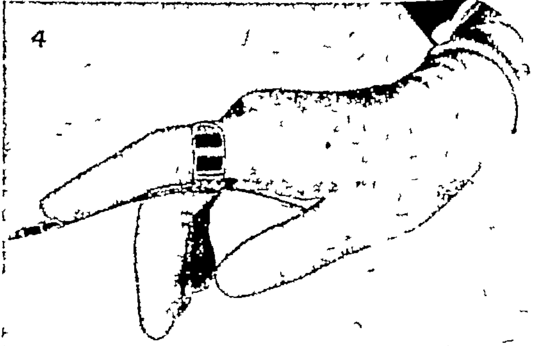


Fig 1—Ring with rotating mechanism

Fig 2—Safe position (cutting edge towards index finger) for entering leaving atrium

Fig 3—Cutting position for dividing lateral commissure

Fig 4—Cutting position for dividing medial commissure

te that in actual use a second glove is worn with its index finger cut away at the level of the terminal interph

* The valvotome handle is marked on one side to indicate the position of the cutting edge

THE LANCET
ONDON SATURDAY, JAN 15 1955

# Mental Health and Public Health

RE was a time not so long ago when mental could be discussed only in terms of woolly lence A fine thing we all agreed, but how did one come by it? It would be nonsense end that we have since learnt how to produce bundance within a generation but at least ve some hypotheses, based on observation and nent which deserve to be tested Thus we eason to suppose that the newborn infant and ther (or her substitute) form a unit and that rmal development of the child depends on being kept together We also think that an le or over anxious or unloving mother may her child's development unfavourably, and rmore that she may herself be all or any of hings because her relations with her own parents unsatisfactory We recognise that no man is nd (for the mental health of all of us is bound th our experiences as members of a group), iat, while any of us may break down under too stress, like an ill used machine, yet, unlike a ne, most of us have the power to adapt ourselves ere stresses, and to a very wide range of them led we have some inner security and are given to make the adjustment Since we are born uble as the sparks fly upward, this last capacity cially valuable for our health of mind Besides worth remembering that if we are influenced ur surroundings our surroundings are also nced by us both are plastic

r the past century the public-health movement outstanding example of man's influence on his ndings—has measurably altered the physical of our people for the better, and no doubt indirectly prevented some mental ill health as But mental health has never been a definite in British public health campaigns and so of this we the pioneers are now some way d other countries in this respect For instance 142 Dr JEAN MACLENNAN and Miss MURIEL L describe how mental hygiene is taught in ouver and it is noteworthy how large a part well trained public-health nurses play in the mme In the United States mental health ing is now a widely accepted duty of public h departments Dr GERALD CAPLAN[1] reports for more than three years the department of nal and child health of the Harvard School of c Health has been successfully exploring the bilities of a team approach to the provision of services for the family, beginning early in the first pregnancy The team (consisting of lists in obstetrics pediatrics nutrition psychi social work and public health nursing) tries to er in the initial stages any physical or emotional s which might disturb family health and ity and to remedy them before they have done s harm CAPLAN[2] has had previous experience of this work as psychiatric director of the Lasker mental hygiene and child guidance centre of Hadassah, Jerusalem Here the problem of teaching was complicated by language difficulties and by the widely different standards of culture of mothers attending the centre yet group discussions kept on a simple emotional plane, dealt with all sorts of topics raised by the mothers themselves—fear of giving birth to monsters fear of the evil eye, fear of dying fear of having too big a baby sexual problems during pregnancy desire for abortion, fear of a second birth when the first was difficult worries about household management and about the other children, sudden aversions towards husband and family, and sudden swings of mood Apart from these discussions short talks were given in the course of which the mothers were warned how common it is to feel no love or warmth to the baby for a few days or weeks after the birth, and were assured that this coldness passes These simple measures it was found not only relieved the emotional tensions of the normal pregnant women but revealed those who were more deeply disturbed and needed individual treatment There are divisions of mental hygiene and psychiatry in the school of public health both at Yale University and at Johns Hopkins—where the programmes of teaching and field demonstration are extensive (Nothing comparable is to be found in any public health school in this country) In the Netherlands too the teaching of mental health, and the training of public health staff for this work is well developed Dr A QUERIDO who is both the chief of the public health section of the municipal health service of Amsterdam and professor of social medicine in Amsterdam University speaks of mental hygiene as an integral part of public health care[3]

These instances suffice to show how far other countries have advanced beyond us in the teaching of mental health There are however some stirrings of life in this field, even here Thus Prof ALAN MONCRIEFF urged as long ago as 1950 in his Dawson Williams lecture,[4] that maternity and child welfare centres should take up the duty of teaching mental hygiene and he pressed for it again in his Newsholme lectures[5] We have recently commented[6] on the report of a London County Council study group, set up by Dr J A SCOTT medical officer of health for the County of London. They made the same proposal and suggested how it might be done and their views were supported by a cogent plea from Dr HEDY SYMONDS[7] who gave examples of the types of family situation which such teaching might ease In Edinburgh (p 160) there is to be a campaign to educate the public in the true nature of mental illness and to encourage the recruitment of nurses But these seedling endeavours make but a small showing on the bareness of the land

The original public-health movement had to fight the inertia of the whole community, and those who now wish it to cover mental health meet it seems some degree of inertia within the service itself For this the curriculum for the diploma of public health is partly responsible So little attempt does it make to orient the future medical officer of health to this aspect of his duties that he is often less well informed about mental health than a recently trained health visitor Indeed, a British nurse engaged in public-health work, who attended one of the W.H O seminars on the subject, remarked ruefully that she did not know how she was going to get the mental-health point of view across to the doctor under whom she was working In saying this we do not, of course, imply that the training of health visitors in mental health is by any means perfect both their training and that of the future medical officers of health requires revision and reorientation if this work is to be done , and courses are also badly needed for those already engaged in this field Proposals for such instruction regularly encounter opposition from those who have matured in another tradition " what," these are inclined to ask, " can anyone tell us about the management of mental-health problems which we are not already doing on common-sense grounds ? " But it is also usual, as a course proceeds, for this resistance to melt the very common-sense of the participants leads them to accept the new approaches opened up for them Nevertheless, as Prof G KRAUS[8] has suggested, where resistance is strong it may be wise to begin by training a few people only—choosing those least at odds with the notions of psychiatry—and leaving them for a time to leaven the lump of their co-workers

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[1] *Children*, 1954 1 171
*Mental Hygiene* 1951 35 41

[3] European Seminar on Mental Health Aspects of Public Health Practice Amsterdam 1953 Geneva World Health Organisation Regional Office for Europe Palais des Nations 1954 Pp 156 Not for sale

[4] *Brit med J* 1950 ii 95
Child Health and the State London 1953

[6] *Lancet* 1954 ii 1005
*Ibid* p 1010

" What is there to teach, anyway ? " is another frequent question, and a far-reaching one , and the tentative suggestions of the L C C study group hardly begin to touch on the answer Of course the first months and years of life are important , of course the mother can do much in those years to make or mar the emotional development of her child and his subsequent mental health , and of course the maternity and child-welfare centres should accept the responsibility for teaching her what to do and—equally important—what not to do But the causes of mental ill health do not all begin to operate at the birth of the child some begin much earlier Dr G R HARGREAVES,[8] whose paper we published recently, shares CAPLAN's view that mental-health teaching should begin in the antenatal clinic, in time to allay the fears and anxieties of the mother during her pregnancy Such fears, when disregarded, sometimes end in psychosis or severe neurosis which may demand months or years of treatment At an earlier stage, HARGREAVES says, the symptoms are still plastic, and simple measures may tip the balance towards adjustment and recovery Many fears of the pregnant woman are absurd and archaic, but they are none the less alarming on that account it does no good, and may do harm, to pooh-pooh them Many of her anxieties, on the other hand, are well grounded, centring on the change in human relations which the birth of a baby brings to every family Quite simple teaching at the antenatal clinic, as well as group discussions of the kind suggested by CAPLAN, can help the mother at this time , and even the obstetrician, as HARGREAVES suggests, should be able give such help, and be willing when necessary to the collaboration of a psychiatrist in bringing mother, whole and safe, through pregnancy, labour, and the puerperium Indeed, QUERIDO that the duty of the public-health service to pre mental ill health runs throughout the lives of one of us, and should properly embrace infants, preschool and school children, young peo work, university students, those in their working women at the menopause, and the aged, as those whose mental well-being is assailed by hazards—such as patients discharged from tal hospitals, people living in overcrowded unmarried mothers, those discharged from young delinquents, the disabled, and those from diseases (such as tuberculosis and ve disease) which affect their lives in the Much of the work done by our public already has some bearing on the mental hea many of these people the children's officer psychiatric social workers, and the probation are all aware of this side of their efforts W now needed is to make what is implicit outsp and to extend the principles of mental hygien every part of public-health work It is an task not only our slums but our mental ho are overcrowded, and more of us are now hampered by neurosis and other forms of ill health than by the diseases which sp lack of sanitation Our sickness has changed public needs rather than tradition should now the pattern of our public-health service

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[8] *Ibid*, Jan 1 1955 p 39

## Pulmonary Hypertension

PULMONARY hypertension is now a well rec disorder, but much remains to be discovered abo ætiology Usually it is a complication of car pulmonary disease, but occasionally it is found absence of either The normal pulmonary resistance is low, and the pulmonary-artery is less than the systemic, even in the presence siderable variations in pulmonary blood flow nary hypertension can result either from a increased pulmonary blood-flow (such as occ a large patent ductus arteriosus) or from an in the pulmonary vascular resistance So more than one mechanism operates in th patient, as in patent ductus arteriosus with na of the pulmonary arterioles In mitral stenosis tension in the lesser circulation may result eit an increase in pulmonary venous pressure the increased resistance at the mitral valve, or increase in arteriolar resistance Severe pul arterial hypertension is always due to red the pulmonary vascular bed at the pre cap arteriolar level The causes of this be obstructive (as in repeated pulmonary various forms of pulmonary arteritis, or cal or secondary to pulmonary fibrosis or emp

Problems in the elucidation of pulmonar tension centre mainly around the mechanis sible for reduction in the lumen of the arter for the organic changes which may also be It has been known for some years that acute can cause pulmonary vasoconstriction and pulmonary-artery pressure [1 2] Thus

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1 von Euler, U S , Liljestrand, G *Acta physiol* 12 301

2 Motley, H L , Cournand, A Werkö, L. Hi Dresdale, D *Amer J Physiol* 1947, 150 315

ıportant in patients with pulmonary heart-
ɔ, in whom the pulmonary artery pressure rises
nitantly with a fall in arterial oxygen saturation
; an acute respiratory infection although
ıtion of the arterial saturation to normal is not
s followed by a fall in the pulmonary artery
ıre [3] In pulmonary fibrosis and in emphysema
ished elasticity of the lungs and destruction of
nall blood vessels reduces the vascular bed and
ses the resistance, uneven ventilation causes
ı, and tends to perpetuate a vicious circle which
n established pulmonary hypertension and right
icular failure In addition to hypoxia drugs
ıs noradrenaline may cause arteriolar constric
while tolazoline hydrochloride ('Priscol') has
said to lower the pulmonary vascular resistance
mary pulmonary hypertension [5] GILMORE et al [6]
suggested that the pulmonary vessels in man are
: autonomic control, but this view has been
ınged by LEE et al.[7] Heart-disease accompanied
n increase in arteriolar resistance may be con
ıl or acquired Organic changes in the arterioles
ıg to reduction in their lumen are common in
ıt ductus arteriosus and in ventricular septal
t, but less so in atrial septal defect [8] EVANS [9]
demonstrated arteriolar endarteritis in such
and on injection of the lungs post mortem
ound 'pruning" of the terminal branches of the
onary tree Arteriosclerotic and other organic
iolar changes have also been shown by other
ers [10 11] The cause of such changes is unknown
s and EDWARDS [12 13] have found that the fœtal
of pulmonary arteriole (in which the lumen of the
l is less than the transverse diameter of the
l wall) may be present in the Eisenmenger
rome, and have suggested that the high arteriolar
tance so produced constitutes a protective mecha-
which prevents the lungs from being flooded with
l under high pressure in this and other congenital
ders In patent ductus arteriosus the pulmonary
y pressure may become so high that the shunt
ses or may cease entirely

the realm of acquired heart-disease mitral
osis is one of the most usual causes of pulmonary
rtension Increased arteriolar resistance is
mon, and has been shown to be due both to
nic narrowing [14 15] and to reversible or functional
owing [16 17] Narrowing is not confined to the
ioles it has been shown by angiocardiography
cour in the small muscular arteries [18] The cause of this arterial and arteriolar narrowing is unknown, possibly it is induced in some way by the elevated left auricular and pulmonary capillary pressures. Anoxia may be a factor, since oxygen inhalation has been shown to lower the resistance [19] WOOD [20] has found that in mitral stenosis with a very high pulmonary vascular resistance there is right ventricular insufficiency rather than pulmonary congestion Arteriolar constriction is now usually regarded as a protective mechanism which shields the pulmonary capillaries from the powerfully acting right ventricle [17 21] but this view has been challenged by DAVIES et al [22] These workers have shown that in mitral stenosis the total pulmonary vascular resistance can be reduced by hexamethonium bromide without producing pulmonary congestion or œdema, and they claim that attacks of pulmonary œdema are commoner in patients with an increased vascular resistance than in those without Unfortunately their data are not sufficiently complete to show conclusively that hexamethonium acts solely by dilating the pulmonary blood vessels through a reduction in arteriolar resistance, reduction in systemic as well as pulmonary resistance may play a part [23] While it seems likely that an extreme arteriolar resistance shields the pulmonary capillaries at the expense of the right ventricle, this may not always prevent pulmonary œdema nor is it necessarily beneficial

In recent years there have been many reports of pulmonary hypertension due to an increased arteriolar resistance in the absence of congenital or acquired heart-disease or of pulmonary disease In 1940 DE NAVASQUEZ et al [24] described cases of right ventricular hypertrophy of unknown ætiology in which the pulmonary arterioles were normal at necropsy DRESDALE et al [5] in 1951 reviewed "primary" or "essential' pulmonary hypertension which predominantly affects young people and is characterised by symptoms and signs of severe pulmonary hypertension due to a high arteriolar resistance without any cardiac or other pulmonary disease WOOD [21] drew attention to the occurrence in this disorder of tiredness, dyspnœa syncope, and even angina of effort and of a small pulse and cold extremities a giant a wave in the jugular venous pulse right ventricular hypertrophy, narrow duplication of the second heart sound with accentuation of the pulmonary element and sometimes pulmonary systolic or diastolic murmurs Cardioscopy shows enlargement of the right auricle, ventricle and pulmonary artery, with clear peripheral lung fields The electrocardiogram shows distinct right ventricular dominance The arterial-oxygen saturation is initially normal but may become slightly reduced as the disease progresses yet cyanosis, when present, is usually peripheral Recently CUTLER et al [25] have described seven patients with this disorder which they have designated the pulmonary vascular obstruction syn

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23 Storstein O., Tveten, H *Scand J clin Lab Invest*. 1954 6 169
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drome All had extremely high pulmonary arteriolar resistances, and at necropsy in two of the cases the pulmonary arterial tree showed patchy atheroma, the large elastic branches having hyperplasia of the media with duplication of the elastic lamina and slight degenerative changes The muscular pulmonary arteries were the seat of pronounced subendothelial fibrosis, often occluding the lumen, many were obliterated by thrombi The capillaries and veins were normal GILMOUR and EVANS[20] described endarteritis fibrosa in the muscular pulmonary arteries in a case of primary pulmonary hypertension, and concluded that these changes might be secondary to the hypertension Necropsy studies in other series[24] have not always revealed any definite vascular abnormality, and DRESDALE et al[5] considered that the anatomical changes present in some cases might be secondary to neurogenic vasoconstriction Cor pulmonale due to multiple pulmonary emboli has been described,[27] but CUTLER et al[25] do not regard this as the cause in their cases They suggest that an extremely high arteriolar resistance in congenital heart-disease (particularly ventricular septal defect) may be due to a separate, possibly genetically determined, pulmonary vascular disorder WOOD[21] emphasises the rapid progression of primary pulmonary hypertension, but the condition of two of the patients described by CUTLER et al did not deteriorate for twenty to thirty years They mention the risk in such cases of sudden death, and remark that these patients tolerate any diagnostic procedure badly, one of their patients died suddenly during cardiac catheterisation

The organic arteriolar changes found in severe pulmonary hypertension, from any cause, have features in common the factors responsible for arteriolar constriction may also be similar Until this mechanism is known much will remain obscure, but studies with drugs which cause arteriolar dilatation may yield further important information Further examination of the bronchial circulation may also throw light on disordered function of the pulmonary vascular system[28] Meanwhile it is useful to remember that the clinical picture of severe pulmonary hypertension is remarkably constant, whatever the cause, and resembles that of the "essential" type, especially in patent ductus arteriosus where the flow may be reversed and the typical murmur absent, and in mitral stenosis where the diagnostic auscultatory signs may be negligible or absent as a result of the greatly reduced flow through the mitral valve Treatment of the pulmonary vascular obstruction syndrome is unsatisfactory, except in mitral stenosis where successful valvotomy may be followed by a fall in vascular resistance,[20] and in patients with a patent ductus which has been ligated before the shunt has ceased or reversed Accurate diagnosis, which is often possible only by cardiac catheterisation or angiocardiography is therefore essential For the rest, treatment with vasodilator drugs, such as tolazoline or methonium compounds,[5 21 22] may be worth trying

# The Fertility of British Women

THE fears so often expressed about the

of our population and the decline of our birth

led to the appointment of a Royal Commissio

Population[1] whose final paper, on the trend

pattern of fertility in Great Britain, appeared

week[2] Though "planning" is a word which

lost a little of its pristine savour, some intel

predictions must be made about the results of p

trends in fertility and family size if our

are to be anticipated and resolved To obtai

basic data, the commission asked Prof D V G

and Prof E GREBENIK to undertake a family

encompassing more than a million women in

United Kingdom Their report on this

conducted in 1946, has interest as much for

discussion of methods as for the results

This survey, supported by none of the legal

of a national census, relied entirely on the coöpera

of individual women, public relations were then

vital Press and B B C publicity was consid

and in the main helpful, though some papers

against "snooping" which was "entirely rep

to the British sanctity of the home which has b

been our national heritage" On the day,

tenth reference leaf was drawn from the alphab

ration-book file at every food office in Great B

From that sheet the names of all apparently m

or widowed women were extracted, and questi

were despatched to them by post These

who formed a representative 10% sample of

national total, were asked to report their m

status, the number and dates of birth of their chi

and their husband's occupation Thirteen thou

locally recruited enumerators called on them

to collect and check on their replies In all

inquiries a high response ratio is essential to suc

and for a voluntary inquiry of this type, the

reply was remarkable A personal letter from

chairman of the commission, emphasising the

ance and confidentiality of the inquiry, pro

a response from some of the more reluctant

contact could be made with women who existed

in the imagination of those who profited by

ration books, while in some sections of London

was little hope of finding women "at home"

accommodation address, even in the required

calls In the second week of the census came

announcement in the House of Commons

end of the supply of dried eggs and the cost

family census stirred up adverse comment, an

caused a sharp acceleration in the usual increase

non response rate which comes with deepening

and resistance Response-rates differed ac

to the region of the country, surprising

Northerners proved particularly docile,

worst response-rates were in the larger urb

where problems of contact were greatest C

tion depended, above all, on the interviewer,

best when he combined previous experience

subtlety of approach—as in the enumerato

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26 Gilmour, J R, Evans W J Path Bact 1946 58 687

27 Owen W R Thomas W A Castleman B Bland, E F New Engl J Med 1953 249 919

28 hand P Gilroy, J C Wilson, V H *Thorax* 1950, 97

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1 Report of the Royal Commission on Population H.M Office 1949 See *Lancet* 1949 i 1105 1110

2 The Trend and Pattern of Fertility in Great Britain on the Family Census of 1946 by D V GLASS and E G Part 1 Report Part 2 Tables H.M Station 1955 Pp 306 and 253 70s the pair

led to the sense of solidarity of the working s by pleading that he was only trying to earn onest fifteen coppers which were paid for each leted schedule Corrections were made for the differences between regions and population ties by duplicating or rejecting records at om so as to bring local response-rates into line the national average of 87 5%

me cross-checks between the results of the family s and national vital statistics convinced the ors that the sample obtained was in fact reason representative, and that conclusions could be y based on it The survey showed that between and 1925 the number of live births per woman ned by 62% from 5 8 to 2 2 More striking ps is the virtual elimination of the large family e late 19th century three fifths of all families sted of five or more children but in the 1920s families were of only one or two children childlessness had doubled in frequency Fertility s with age at marriage and with social class ough the professional classes, with their small lies do tend to marry late, late marriage does ully explain the rise in family size from 1 6 among ied employees and 1 97 among non manual -earners to 3 35 among industrial labourers Indeed, age at marriage and family size are related only in so far as they are both expressions of the complex of social attitudes which distinguish one class from another That these social attitudes are not fixed and immutable is shown by the changes in reproductive behaviour even within the same social grouping in the last fifty years, the wives of employers married in the '90s had just as large families as the wives of unskilled labourers married in 1920–24 Again not only have families become smaller but the space of years in which families have been completed has contracted, and the birth rate has fallen most notably in the period after the first ten years of marriage

Long range population predictions are at best an educated guess GLASS and GREBENIK are therefore cautious in their projection of future trends from past events, but they point out that ultimate family size which fell steadily up to 1930 and maintained an uneven stability thereafter now shows a slight upturn Because of the improving mortality experience and realisation from these data that family limitation is already widely practised in all social classes they feel reasonably confident that continuation of current fertility rates will achieve the desired effect of population stability

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# Annotations

## CEREBRAL ARTERIAL DISEASE

ERE has long been uneasiness about the classification congenital defect of the change underlying rysms of the circle of Willis This concern was d most strongly by Glynn[1] who pointed out that e circle of Willis congenital defects were eighty as common as aneurysms Some additional factor sisted, must be involved in the formation of ysms. He showed that the defects were not in weak spots and did not bulge or break when after the vessels were overdistended at pressures about times the normal systolic pressure The fact that were far commoner in adults than in infants does xclude a congenital origin, since growth and rise ood pressure could make manifest minute funda l defects. In fact berry aneurysms are associated coarctation of the aorta and polycystic kidneys[2] ditions in which there are hypertension and other nital defects. Forster and Alpers[3] have recorded ase of a 13 week-old infant with unruptured ysm and polycystic kidneys This strongly suggests ngenital origin—a clear cut malformation of the possibly through the mechanism described by whereby the many small vessels present in the embryo fail to concentrate into the one main of the normal adult This is in keeping with the ation that abnormalities of the circle of Willis ore usual in patients with aneurysms than in those t If this is really the mechanism the congenital nality is the whole aneurysm not merely the ess in the wall hypertension enlarges and may o the persistent abnormal vessel but it is not y responsible for the formation of the aneurysm a minor defect Handler and Blumenthal[4] have ed inflammatory changes in the basilar artery and suggested that these are related to the formation of aneurysms[4] This does not accord readily with the usual picture of a clean break in the aneurysmal wall Moreover the basilar artery is not a usual site of aneurysm and no exciting causes have been found for this peculiarly local inflammatory reaction The well known mycotic aneurysms of infective endocarditis are clearly unrelated to the aneurysms which are the usual source of subarachnoid hæmorrhage The reaction seen by Handler and Blumenthal is probably secondary to local degenerative plaques

Current ideas on atheroma have been severely handled by Duguid and by Crawford who have shown the inadequacy of the hypothesis of simple lipoid imbibition and secondary medial changes from pressure Blumenthal et al[5] have taken up the question of localisation of atheromatous patches in the larger cerebral arteries Although the total quantity and distribution of atheroma in various arteries may vary enormously if present it occupies standard places and configurations; and Blumenthal and his colleagues have shown a correlation between tension on the wall and plaque formation They do not appear to have fixed the arteries they measured in a state of distension to the normal pressure Crawford and Levene[6] have shown the great difference this makes to the picture the apparent bulge of atheroma into the lumen is then replaced by a bulge into the media The problem of atheroma is thus being approached from two angles—the metabolic and the mechanical Blumenthal clearly regards arteriosclerosis as an adaptive response rather than a primary degeneration: the bulky local accumulations of fatty material would follow rather as aberrations of repair than as defects in normal intima and the prevention of atheroma would have two steps—the avoidance of strains in the arterial wall requiring repair, and the avoidance of lipoid accumulations in these areas of repair The two parts of this mechanism which are not necessarily related, fit the known correlations of atheroma with increased blood lipids and with prolonged arterial hypertension.

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[5] Blumenthal H T Handler F I Blache J O Amer J Med 1954 17, 337

[6] Crawford T, Levene C. L. J Path Bact 1953, 66 19

## THE RESTFULNESS OF CHANGE

> "Volumes are now written and spoken upon the effect of the mind about the body Much of it is true But I wish a little more was thought of the effect of the body on the mind"

IN setting down this perennially modern reflection, Florence Nightingale[1] was considering the havoc a sick body can play with mood and judgment Those who "think that 'with a little more self control' the sick might, if they choose 'dismiss painful thoughts' " fail entirely, she held, to realise what they are asking of the patient "Almost every step that crosses his room is painful to him, almost every thought that crosses his brain is painful to him, and if he can speak without being savage, and look without being unpleasant, he is exercising self control" It is therefore the business of his attendants to alleviate his depressed and irritable state by satisfying the "craving for variety in the starving eye"—giving him not merely a "judicious variety" of flowers, but a pleasant view, and pleasant things about him.

We do not give much thought to this principle in hospitals nowadays Flowers are certainly present, but there is little other attempt to provide variety hygiene, in fact, has ridden roughshod over psychology The patient in the public ward suffers less in this respect than the patient in the private ward for the patient in the public ward can at least refresh his eye with a variety of nurses, a variety of fellow patients, and a variety of nursing techniques as well This may not be quite what Miss Nightingale had in mind, but they are better than the blank wall set with glazed lavatory tiles which often confronts the patient in a private ward The craving for the return of day, she suggested, is often nothing but the desire for light, "the relief which a variety of objects before the eye affords to the sick mind" When these objects lack variety the mind gets no respite, and to this she attributed the depression so commonly seen in the chronic sick "subjected to a long monotony of objects about them" She might have added that the daily inspection of a blank tiled wall sometimes suffices, within a week or ten days, to convert a convinced optimist into a practising pessimist

Would she had thought that the need for variety (with a small "v") is sufficiently met by the broadcast programmes dispensed to hospital patients? It is doubtful, for, like so many of us, she seems to have been a "visual type," accounting sight the prince among the senses Does television perhaps supply the kind of nourishment the eyes of the sick crave? It is difficult to place a television screen so that all the patients in a ward can easily see it and there will always be some for whom the content of a given programme lacks appeal

Miss Nightingale proposed, as she so often did for other problems, a simple and practical solution The ward, whether public or private, is no place for a medley of agreeable knick-knacks, on the other hand its walls offer ample hanging space for pictures, and these can be changed The changes need not be made unduly often she pointed out that if you show a patient ten or twelve pictures in rapid succession you merely make him tired or feverish, "but hang one up opposite him, one on each successive day, or week, or month, and he will revel in the variety"

Some hospitals—but not many—have already had frames fixed to the walls into which pictures can be slipped, and they either keep a supply of good reproductions which are placed in these frames in rotation, or else they make use of the circulating library of pictures provided for hospitals by School Prints Ltd[2] This service was established about a year ago, and is steadily supporters

School Prints send a set of six pictures at a time, m on hardboard and varnished (but unglazed), so edged th have the appearance of being framed They are thu to collect little dust, and are in any case easily wiped o a damp cloth Each carries a small neat label giving th of the picture, the name and nationality of the artist, a dates Each set of pictures includes one showing p portrait or a scene with characters), two landscapes, tw river scenes, and one decorative subject, one at least o is by an old master, and the rest are by later or living At the end of four months a new set of six pictures and the original six are packed up and sent off to th hospital on the rota

Some hospitals—Orsett,[3] in Essex, for instanc had murals painted, which give gaiety and variety t wards Miss Nightingale, rightly or wrongly, that such refreshments to the mind act also on the "Little as we know," she wrote, "about the which we are affected by form, by colour and do know this, they have an actual physical effect of form and brilliancy of colour in the objects to patients are actual means of recovery" She capital observer, and her advice, even after a years' delay, is well worth taking

## DEFORMITIES OF THE CHEST WALL

CONGENITAL deformities of the anterior chest naturally into one of two groups—the pro the depressional The protrusional deformity is due to rib overgrowth When this is bilateral the protrudes, when unilateral the ribs are unusually nent at the costochondral junction Patients type of deformity have restricted chest expans movement of the diaphragm may also be affected deformity may be treated surgically either by osteal resection of the sternum, or by resection costal cartilages, after which regeneration is al occur in the normal position Lester[4] has descr cases in which patients underwent operations of this and he assesses the results as largely satisfactory

Depression of the chest, which is commoner, is associated with shortening of the central tendon diaphragm and backward curvature of the st Evans[5] has studied the cardiac changes asso this deformity Most of the patients have a murmur and an abnormal cardiac outline on ra associated with narrowing of the space between and thoracic vertebræ Lester has operated patients with sternal depression In infants the def may be relieved by excision of the xiphoid and costal cartilages In children and adults a more operation is necessary The 3rd–7th costal ca are resected, and a transverse wedge osteotomy across the 3rd sternal segment The xiphoid is and the body of the sternum elevated The stern be retained in position either by stainless steel passed behind it and tied to an anterior supp by using a section or rib as a strut[6] The results 90 operations are said to be functionally good patient died and 4 required reoperation In this Chin and Adler[7] have operated on 10 patien funnel sternum They suggest that operation sh advised for all children over the age of 6 months, adults with symptoms due to this deformity Th that the sternum can be freed from the diaphra after osteotomy can be retained in an over-co position without external fixation The costal ca are removed if they are deformed

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d Writings of Florence Nightingale Compiled by LUCY SEYMER M A S.R.N New York and London illan 1954 Pp 397 35s

comb Street, London S W 1

3 *Lancet* 1947 i 840
4 Lester C W *J Amer med Ass* 1954 156, 1063
5 Evans W *Brit Heart J* 1946 8, 162
6 Dailly J E *J Amer med Ass* 1952 150, 1203
7 Chin E F, Adler, R H *Brit med. J* 1954 i 10

any years must pass before the results of such ations can be assessed If the depression is really to shortness of the diaphragm, then the deformity recur as the fibres of this muscle find a new chment and if they fail to become reattached herniation may ensue In few patients are the symp s due to funnel sternum severe enough to demand ical relief although operative correction may nately be justified on cosmetic grounds alone

## ATTEMPTED SUICIDE—AND AFTER

atchelor and Napier[1] have followed up for a year fate of 200 patients who had been admitted to an rvation ward in an Edinburgh general hospital for mpted suicide They traced all but 1 and their ings should be valuable not only to psychiatrists to general practitioners Their series comprised men and 108 women the commonest diagnoses on ission were 'depressive state' (41 men 71 women) psychopathic state (25 men 17 women) epilepsy zophrenic and paranoid reaction organic reaction s, and mental defect contributed much smaller bers. The ages ranged from fifteen to over seventy the largest number for any decade was 48 (22 26 women) aged twenty to twenty nine though next three decades with 38 (17 men 21 women), 17 men, 14 women) and 37 (16 men, 21 women) well represented 106 patients (53%) were kept in general hospital for a week or less 69 (34 5%) for to two weeks, and 25 (12 5%) for longer Of this group three fifths were discharged home 6 (3 men men) died in the observation ward 3 from advanced se of the central nervous system, and 3 from respira or cardiovascular disease Of the remaining 194, (51 men 63 women) were discharged home 48 (21 , 27 women) were transferred as voluntary patients ental hospital and 7 (2 men, 5 women) were trans ed under certificate; 22 (13 men, 9 women) were sferred to a neurosis clinic or nursing home; and r disposals totalled 3

% of patients were discharged home compared 57% also in Hopkins's[2] series and 20% in Stengel's[3] helor and Napier point out that the majority were arged home after less than a fortnight in the observa ward but each case was thoroughly investigated and continued to attend under their care as outpatients believe that their rather free policy was fied by its results. During the year 4 of the patients mitted suicide and 3 of these had been in the mental ital the 4th suicide and 7 other patients who made er unsuccessful suicidal attempts belonged to the ically temperamentally unstable group for whom ave at present no effective treatment or suitable ision The Edinburgh workers consider that al hospital care is needed chiefly for attempted les with depressive schizophrenic, and paranoid oses and more often for those past middle age for young people automatically to send every pted suicide into a mental hospital is not only essary but wasteful of mental hospital beds But emphasise the serious suicidal risks accompanying epressions of late middle age and of old age, especially the depression has been initiated by the breakdown relationship characterised by intense possessive with resultant hostility towards the loved person g to severe guilt feelings At the close of the only 13 5% of the patients were in mental hospital; were at home and 59% were at work

cussing social reverberations, Batchelor and r agree with Stengel that in some instances attempted suicide may be in the nature of an appeal to family or friends to come to the rescue when the patient is at his wits end but they point out that some melancholics seem completely self absorbed They insist that the patient who has attempted suicide needs not only a chance to recover in a sheltered environment but help in fitting himself once more into his social setting The near relatives, too may need help; in many cases the disturbance to the family dies down quickly but in about 15% of cases the families were emotionally dis turbed for some months 3 relatives had to be treated psychiatrically and 1 woman tried to commit suicide seven months after her sister had done so

It is a pity that this excellent paper does not include data on social and family background or marital status which must surely have influenced Batchelor and Napier in their 'rather free policy' but no doubt they will further explore the lode they have opened up

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chelor I R. C. Napier M B J Neurol Psychiat 1954 17 11
pkins F J ment Sci. 1937 83, 71
ngel E Proc R Soc Med 1952 45 613; see Lancet 1952 1059

## GENITO URINARY INFECTIONS WITH HÆMOPHILUS

MANY bacteriologists will learn with surprise of the claim by Gardner and Dukes[1] to have isolated a new bacterium which they regard as the cause of most cases of non-specific vaginitis. They state that a previously unidentified and unclassified hæmophilus has been isolated as the predominant or only organism from 81 of 91 such infections From a clinical study of the cases in 62 of which the hæmophilus was the only organism present Gardner and Dukes report as evidence of a specific disease-entity that the vaginal discharge is grey thin homogeneous offensive in smell and less acid than normal vaginal secretion and that itching and irritation are seldom prominent They reproduced the disease in volunteers by direct inoculation with infected vaginal material and pure cultures of the hæmophilus Direct films of the discharge showed abundant, short, pleo morphic, gram negative rods which could be cultured with some difficulty in an atmosphere of carbon dioxide and only on 'proteose peptone No 3 agar' containing 10% sheep blood The organism was sensitive to the tetracycline group of antibiotics and to sulphonamides Administration of these drugs by mouth or into the vagina eradicated most of the infections. A complete account is to be published[2] and most will prefer to reserve judgment about the novelty and the causal rôle of the hæmophilus until the full report has appeared

Meanwhile, the brief description of the organism inevitably recalls a rather similar account by Leopold[3] who reported the frequent isolation from urine and cervical swabs by strikingly similar cultural methods of a hæmophilus which was hæmolytic In males the presence of the organism in the urine was associated with mild prostatitis with or without urethritis; in women there was an association with cervicitis. Leopold found the organism in the urines of 53 of 905 unselected men and of 2 of 18 men with a previous history of non specific urethritis in 16 of 58 cervical swabs; and in the urines of 4 of 9 men whose wives had positive cervical cultures

Few bacteriologists nowadays expect to discover a hitherto undescribed bacterium as the cause of an infec tion But possibly they have too readily abandoned this type of search to the virologists There is some danger of discovering only the bacteria that are expected in any disease process because the methods of culture applied are those best designed to isolate such organisms and to discourage as many others as possible. Whatever may be the final judgment of the new claims there would seem to be no insuperable difficulty in the way of attempting to repeat the observations of Gardner and Dukes

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[1] Gardner H L, Dukes C D Science 1954 120 853
[2] Amer J Obstet Gynec (in the press)
[3] Leopold S U.S. Armed Forces med. J 1953 4 263

## Special Articles

# THE WORK OF A MENTAL-HYGIENE DIVISION IN A PUBLIC-HEALTH DEPARTMENT

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THE view is now widely accepted that mental hygiene is the proper concern of a public health department The prevention of all forms of preventable illness and disability is the natural aim of a truly comprehensive public health service Within the scope of such a comprehensive service come many forms of psychological and emotional disorder The methods of prevention of psychiatric disabilities are various, for they are not yet as well tried and standardised as those used in the prophylaxis of infectious diseases, for example So a description of the functioning of one mental-hygiene division within a public health department may be attempted for reasons of comparison and review

The public health worker is not inclined to invade the already well-cultivated field of psychiatric treatment He would be content to leave therapy with those whose particular interest it is and to concentrate his own efforts upon his own territory in "the recognition and eradication of factors in the community which are harmful to the healthy psychological development of individuals" rather than in "the treatment of the results of those factors"[1] However, psychiatric treatment of children can be very time consuming, and the sooner emotional difficulties and unhealthy attitudes to other people are recognised the more easily they are corrected The natural division seems to be not between therapeutic and preventive services but between clinics which offer intensive therapy and those which offer guidance and "superficial" therapy Furthermore, in staff education in the principles of mental hygiene, case studies under supervision are a sine qua non thus with a basically preventive orientation the public health worker still finds himself doing a fair amount of treatment

### THE METROPOLITAN HEALTH DEPARTMENT

In Vancouver, the mental hygiene division of the public health department was set up in 1939 An integral part of the health department, it functions like an 'enzyme system," permeating the work of other divisions within the department and through them the health of the community as a whole Its activities can be more pervasive than those of a child guidance clinic which operates within an education department and is—administratively as well as in orientation—more confined

The health department is set up on a metropolitan basis to include the spreading urban area of Greater Vancouver The Metropolitan Health Committee, which directs the department is composed of elected representatives from the City of Vancouver and five surrounding municipalities, together with the university area and another smaller area of the adjoining part of the province of British Columbia The population served was estimated, in 1953, at 522,030 The population of the City of Vancouver itself was 390,325 for the same year The whole of this urban and suburban area exceeds over 248 square miles

The work of the health department is centralised in Hall, from which many of the services operate The personal health services and sanitary inspec are directed peripherally from seven "health four of these being within the City of Vancouver other three covering surrounding areas

The total staff of the health department compr professional and lay officials, including 13 full time and time medical officers, 114 public health nurses, 36 inspectors, 19 dentists, 2 psychiatric social workers, logists, 2 nutritionists, and 2 audiometrists, all general direction of the Senior Medical Health Officer

The work of the medical health officers and of the health nurses is diverse, covering school health and kindergartens, child-welfare work and child centres, immunisation and communicable disease (including tuberculosis and venereal disease, in tion with the provincial departments of tubercul venereal disease control) Mental hygiene work out in relationship to these other activities and an increasing amount of time and attention staff meetings are held both in the health units and City Hall

Each health unit is led by a medical health who is the "unit director," and by a senior public nurse, who is the unit supervisor In the large there are also assistant unit supervisors The of public health nurses attached to each unit from 4 to 17 according to the population and each area

### OTHER AGENCIES

The staff of the metropolitan health department school services to the "public schools" (i e, are publicly provided and administered by the of school trustees of the City of Vancouver, and other municipalities of the metropolitan area) mately half the time of the unit directors and other full-time medical officers and of the public nurses is devoted to school work Certain "non schools" are also provided with health service are essentially church schools

The provincial government of British Colum the major health authority, has its divisions of culosis control, venereal-disease control, child guidance, and others in its health de the metropolitan health staff work in close with these The child guidance clinic of the health department has its headquarters in It is more concerned with treatment than is the hygiene division of the local health department, has prevention as its primary objective It understood therefore that these two agencies attract a rather different case-load, and that ca be referred from the metropolitan mental hygiene to the provincial child guidance clinic The of demarcation between prevention and treatme ever, has been somewhat erased, and the local department has assumed perforce a minor "treatment"

The work of the metropolitan health staff assisted by the local medical profession practice and by the hospitals The Health Ce Children at the Vancouver General Hospital larly valuable to the children of the city, pro wide range of outpatient and inpatient faciliti director of the mental hygiene division is an psychiatrist on the staff of the Health Centre for and a director of one of the health units is at its staff as a pædiatrician in the outpatient dep A senior member of the staff of the Health Ce as consultant in cardiology to the metropolit department A public health nurse of the men staff is employed full time in the health ce "liaison" public-health nurse The local health ment is thus linked clinically with the teaching s pædiatric functions and has a small share in raining of medical and nursing students in child

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[1] W H O Technical Report no 9 1950

e metropolitan health department provides instruc to students in various faculties of the University ritish Columbia—including medicine nursing and economics Its staff works closely with the rian Order of Nurses (domiciliary nursing service) Children's Aid Society (child life protection) the social service department (relief of indigents) the pled Children's registry the B C Tuberculosis ety, and many other voluntary and municipal nisations.

### THE MENTAL HYGIENE DIVISION

e staff of the mental hygiene division engaged le-time in this work comprises a director and assistant tor who are specialists in psychiatry two psychiatric l workers (a man and a woman, the latter being a qualified public-health nurse) and two psycholo

The director is also director of the school health ce for the city of Vancouver He and his assistant tor conduct the mental hygiene clinics which operate he various health units The psychiatric social ers are engaged mainly in reinforcing and guiding work of the public health nurses in the schools and s they take a prominent part in staff education[2] psychiatric social workers also carry out individual work on a limited number of cases

o psychologists work very closely with the psychia in the mental hygiene clinic, assisting in the osis carrying out psychometric examinations and ding therapy The psychologists also coöperate the medical officers and public health nurses in in selected child health centres seeing particular referred to them and reviewing the progress of rently normal healthy babies. These members of ental hygiene team work in the closest relationship the public-health nurses medical officers, the unit tors and the unit supervisors The medical officers he public health nurses bring forward the problems he environmental and social data while the staff e mental hygiene division coöperate in furnishing gnosis and recommendations which are carried out by the staff members concerned Thus from the al hygiene division the stream of thought and y and action flows out via the units into the schools ho homes where the children of the rising generation eing educated and nurtured Directly and indirectly school staffs are affected Parent associations are g increasingly into this community of thought gh formal lectures, discussion groups or round conferences other interested bodies are reached church groups racial associations university ences, and others

the periphery the public health nurse and medical go about their daily routine in schools child health s and clinics The work of the public health nurse akes her into the homes of the people through to tuberculous patients young infants expectant rs and others in need of her services Daily ts with teachers and pupils in the schools with rs in the child health centres and with families in homes, keep the public health nurses in constant with the problems and needs of their patients f the referrals to the mental hygiene clinic come e public health nurse or the medical officer they me from the teacher or from the parent to the health nurse in the first place More and more re being referred by private medical practitioners casionally cases are referred by other social

### THE MENTAL HYGIENE CLINIC

The mental hygiene clinic is the main focus of all this activity It is primarily a clinical consultation which culminates in diagnosis and recommendations for treatment but its usefulness is not limited to the needs of the individual case Thus it has a most important educational function particularly for the new recruits to the public health nursing and medical services Where a school child is concerned its impact is felt in the schools for the child's teacher and school principal are usually present when the case is presented at the conference which follows the clinic session

The clinic is held as a rule once a week in each of the health units One psychiatrist and one psychologist are always present and the psychiatric social worker may be present for a varying amount of time Usually 3 cases are dealt with at each session. The consultations and examinations are held in the morning while the case-conferences are convened in the afternoon Those seen are usually school children mainly aged 6 10 In 1953 254 new cases were seen

In the preparation of the case several visits have to be made to the home by the public health nurse, who then prepares a detailed case-history which includes an extensive family history as well as an account of the relationships of the child at home and in school Wherever possible she talks to both parents and in some cases to other relatives living in the home

At an early stage the child is referred to the medical officer if he has not recently seen him The unit director may contact the private practitioner where necessary and the public health nurse is also in touch with other social agencies which may have been concerned with the family (A useful organisation for this purpose is the Social Service Index where social agencies including our own register the names of persons who have applied for advice or assistance) The school authorities are also requested to furnish their report and this is made out in detail by the child's teacher covering academic achievement and social adjustment as well as the results of any intelligence tests which have been given at the school

At the clinic the child and one or both parents are seen by the psychiatrist who includes a full physical examination of the child in his evaluation of the case. Thereafter the child and parents are interviewed separately by the psychiatrist While the parents are consulting with the psychiatrist the child goes to the psychologist for examination and observation.

The relevant findings from these examinations are presented along with the other material data at the case-conference, which is held in the afternoon It is usually possible to indicate the problem in general terms without divulging personal matters which are best left as confidential details on the file

In addition to the staff of the clinic there are present the public health nurse the unit director the unit supervisor or assistant unit supervisor and also any of the following who are concerned in the case—class teacher school principal social worker of any other social agency which may be involved and also occasionally students in postgraduate nursing courses The problem is unfolded usually by the public health nurse or—if the problem has arisen initially in the school situation—the child's teacher and the school principal The psychiatrist as chairman calls on the persons who can contribute to the discussion The psychologist's account is always important In some cases a good deal of the background is known only to the family doctor who is invited to the conference but is rarely able to attend In such cases his report will have been submitted to the unit director The conference may occupy thirty minutes or up to an hour or more the psychiatrist coördinating the discussion and bringing out the main points in diagnosis and recommendations for further action. These are set out concisely but in some detail in the written report which is transmitted by the psychiatrist to the unit director after the conference A copy of this report is sent to all the agencies who may have an interest in the case—e.g., the school or kindergarten, the family doctor the school board and various social welfare agencies

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ry, C H Hunter T G Itkow H Mental Hygiene 37 17

### THE PUBLIC HEALTH NURSE

In the whole mental-hygiene programme, the public-health nurse is the key figure If the mental-hygiene division is a sort of enzyme system, then in order to get the enzymes (or mental-health principles) working actively to bring about change in the classroom and the home, the nurse must take them there Similarly, if the division is to continue to function it is the nurse who must be the case finder, bringing in fresh material for the triple purpose of education, prevention, and therapy Indeed, the main efforts of the whole division are directed towards equipping the nurse more fully for her task, and guiding and sustaining her as she carries it out

1 The public-health nurse is ideally situated to act as a potent force for mental health *in the community*, first because she is there, and secondly because she has in most cases no hurdle to take to be accepted as a "helping person"—she has been that from way back She knows the family in their own setting, and she is aware (or soon becomes so) of their limitations, their difficulties, their weaknesses, and their strengths To translate principles into practice in all sorts of varied situations is her traditional function If, then, she herself is imbued with mental-health principles, equipped with techniques of interviewing, and has a sound knowledge of the dynamics of development and behaviour who can more persuasively teach, guide, and support the parents of the growing generation?

2 *In the schools*, too, where part of her every day is spent, she can help the teachers to understand Johnny's behaviour in terms of his needs, and assist them in attempting to meet these She can make them aware of underlying causes in his background, and thus enable them to deal more understandingly and effectively with him

3 In her work *in the child health centres* she puts the same principles and the same equipment into action In her individual conferences with the mothers she has a unique opportunity to teach the known facts of normal growth and development, not in a remote academic way, but focused on this particular child as he is now For "visual aids" she needs little more than the baby himself It is in this setting, too, that she learns to detect unwholesome attitudes that may lead to later difficulties in the parent child relationship This has been termed "anticipatory guidance," and our attempts to introduce this concept into our baby centres have already been described[3]

4 Mental hygiene is not a tool to be applied to special cases but a way of working in all situations where one deals with people Some graphic illustrations of this have been given *in the field of tuberculosis*

A young married man, father of a small child, had a case history that read like the dossier of an incorrigible All workers had found him hostile and uncoöperative, and he had built up a tremendous hostility towards all agencies, institutions, and workers He refused to carry out any of the procedures outlined for him, or to attend his X ray appointments A new nurse fell heir to him and having read her predecessors reports, decided to seek help before making her first visit She discussed the case with the psychiatric social worker, a member of the mental hygiene division They talked about the possible reasons for this man feeling as he did, and the need to begin with an unconditional acceptance of his attitude, and complete absence of any criticism or attempt at direction The nurse visited, introduced herself, and let him talk—which he did at great length, venting his frustrations, his resentments his humiliations She resisted any temptation to argue, defend, cajole, or coerce At the close of the interview the patient was speaking quietly and with self respect, and ended by asking the nurse to make a ointment for him, leaving the way open for further

The emotional balance of the tuberculosis is almost always affected *to a greater or less* The nurse who realises this, accepts it and h courage and vision to postpone her immediate and apply her knowledge of human behaviour, do more effective work In this field all the knowle skill acquired through her mental hygiene work clinic and in staff education can be put into practic

5 When a case is being referred to clinic her much more formal, time consuming, and ex *The preparation of a case for referral*, and *the su follow-up*, when these are well and truly done, all that a nurse has in the way of observation, know skill, and patience

(*a*) Children are often referred to her by the It may be that a child is not working to capacity, dreaming and withdrawn, or is over aggressive and seeking The teacher discusses the situation with the and pooling their knowledge of the child, they talk of handling it The nurse makes a home visit and after discussion with the principal and teacher it may be to offer the parents the services of the clinic. It wo tedious to dwell at length on the factors basic to this d but briefly they are the nurse's need for further gu the parents' recognition of the problem, their desire fo ability to benefit from help However, this is more ideal, and sometimes cases are brought in where the are obviously a lost cause and plans must be made to help child without counting too much on them. In othe there are some cases—as there are in all big cities—wh prognosis for building family strengths is poor, and must be on therapy for the child

Either before or after the decision to refer the case to the nurse makes a number of home visits during whi obtains the information necessary to write up a fairly hensive social history Writing the history is often re as a tiresome chore, but the nurses have found that the views incidental to this, and the putting together of history itself, clarify the whole problem, and that by the the case comes to clinic both she and the parents have better idea of just where they need the psychiatrist The history varies in length, depending to some extent complexity of the problem and the individual the nurse A social history guide has been drawn up mental-hygiene division to help the nurse in gathering and in constructing the history Help may always be from the psychiatric social worker and the nursing

The nurse takes an active part in the case presenting the case, summarising the details of the personal relationship she has made with the family, and her reasons for bringing the case in Everyone else in, and at the end of the conference the diagnosis is made, and a plan of action agreed upon After whole thing is summarised in the psychiatrist's report, is filed with the history, together with any other matter, such as reports from another agency, and fr child's doctor, and the results of psychometric tests.

(*b*) Unless otherwise decided at the conference, the fo of the case is in the hands of the nurse Occasiona psychiatric social worker may be asked to work wi family on a case work basis, or the case may be han to another agency, for example, the child guidance cl Children's Aid Society, or the Family Welfare Burea great majority of cases, however, it is the nurse wh on, continuing to visit the home regularly, and se interpret and help implement the clinic's recomme both there and in the school This is sometimes on long term basis, continuing throughout the child's sc with progress notes written periodically and reass of the case in clinic as indicated If the family mov child is transferred to another school, the history is to the nurse who takes over

There is a great variation in case loads, of course, in the amount of time and effort spent on the individu and on the work as a whole In addition to all the variables (such as the severity of the problem the re ness of the parents, and the stability of the communit is the temperament and interest of the nurses Som great natural facility for this work, others find it and show more or less resistance, generally due to confidence in their ability to tackle this kind of

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C H, Hall, B E, Hunter, T G *Public Health Nursing*, 1952 ro interested and with the increasing emphasis on this o field, both in preparation and in in service training has been over the years an increasing awareness, ability ureness shown in the nurse s work. For evidence of this has only to glance through the old files and compare the hy history and sparse follow up work of ten years ago those of today One cannot help but be struck by the th in understanding the sharpening of observation and ncreased competence of action, or in some cases the wise holding of action

his outline of the rôle of the public health nurse in mental hygiene work of this agency would not be plete without some reference to *group discussions* more or less informal but regular ' get together few people for the purpose of learning by discussion oing found effective in many fields Arranging discussion is not yet an established part of the lc health nurses' rôle, but the few attempts that been made are very promising Three of our nurses undertaken to ' lead " such parent groups with encouraging response We do not refer here to s to mothers or other groups, but a different freer e living and meaningful process in which the group f is the teacher The nurses and the parents who taken part in these have attested to the real and ng change that takes place in such a setting

f course the pitfalls on the nurse's path as she tries pread the knowledge of the normal and help to ent and correct the deviations from the normal obvious But through the mental hygiene clinic, the lar conferences with the psychiatric social worker or psychologist as her work progresses, and through her experience, the nurse becomes aware of her own ations and those of her agency and learns to work uctively within them. Some there are indeed who o so much of the dangers that they are blind to the ibilities But no-one can deny that mental health blic health and what public-health measure has not with reactionary resistance ? To safeguard against e dangers is one of the functions of the mental ene division

### SUMMARY

n account is given of the work of a mental hygiene ion in a public health department The organisation he metropolitan health department is described. elationships with other agencies are shown The position of the mental hygiene division is briefly hed and the influence of its mental hygiene clinic dicated Examples are given of the ways in which ublic-health nurse exercises her functions in mental ene work (1) in the community (2) in the schools, n child health centres, (4) in tuberculosis control in the mental hygiene clinic and (6) in group ssions

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## BACTERIAL GENETICS

NETICS have an increasing part in the study of riological problems and in order to outline the uses techniques of the subject a colloquium was held in ion on Dec. 14–17 by a group of interested bacteriolo While the range of the discussion was intentionally a medical bacteriologist may have thought that a oportionate amount of time was spent in reviewing enetics of bacteriophage and of *Escherichia coli K 12* his can be justified by the fact these organisms are most susceptible to detailed analysis.

ening the colloquium B A D STOCKER gave an rable review of bacterial transformation and trans on by phage while W HAYES did the same for the ics of *Esch coli K 12* (Unfortunately many of the speakers did not maintain the same standard of ity This was partly because some participants presented new material instead of discussing principles such contributions tended to break the flow of the meeting and the informal air desirable in colloquia was lost ) Discussing the papers by Stocker and Hayes J L JINKS spoke of the exclusion factor which he believes to be an essential part of the mechanism of recombination in *Esch coli K12*

A discussion on population changes was opened by CHARLOTTE AUERBACH who emphasised that workers were sometimes not careful enough in their use of words for instance mutation ' was used to mean both the act of producing a mutant and the mutant itself She also pointed out the dangers in interpreting experiments in which selection of a mutant is involved D A MITCHISON described some of the mechanisms which may bring about large-scale changes in cultures referring mainly to the antibiotics. J YUDKIN sought to explain some of these changes on clonal variation—a hypothesis that would require revision of some of our ideas of inheritance of bacterial characters

The genetics of bacteriophage was next discussed In this field the fact that the result of crosses can be analysed is offset by our lack of knowledge of how the phages are reproduced at present no hypothesis of phage replication adequately fits all the known facts However ELINOR MCCLOY and NEVILLE SYMONDS described the main experimental facts in this field while W HAYES discussed the inheritance of prophage Other viruses were rather neglected but F FULTON did give a satisfying account of the recombination between influenza strains, and he suggested that the virulence of these strains was best attributed to an inherited pattern rather than to any single character

The final session was devoted to some of the applications of bacterial genetics, including its possible uses in the study of virulence T W BURROWS described the importance of growth factors in *Pasteurella pestis* strains while L F HEWITT outlined the rôle of phages in the toxogenicity of diphtheria D ROWLEY put forward a scheme (still in the experimental stage) for analysing the mouse virulence of *Esch coli* strains

The organisers are to be congratulated on their attempt to introduce the *study of genetics to a wider range* of workers.

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## CEREBRAL PALSY

AT the national congress of the Societa Italiana di Ginnastica Medica held in Milan on Dec 6–8 Dr A COLLI GRISONI (Milan) pointed out that there had been a distinct change in the approach to the infantile cerebral palsies Formerly regarded as osteomuscular states, only partly amenable to static forms of treatment, they were rapidly becoming recognised as neurophysiological conditions in the developing child, calling for a dynamic approach Defective development should be evaluated from both physical and mental angles, in order to give a prognosis of a child s educability Her fundamental principles of treatment could be grouped under three heads—physiotherapy occupational therapy and speech therapy—and suitable personnel were about to be trained in Italy for this work Trainees with a vocation must be selected and specially trained in precise techniques of management She felt that babies are best treated at home children between 3 and 5 years at special day centres attached to hospitals and older children at schools for handicapped children She emphasised the importance of instructing parents in day to-day care of their children, and remarked that even children barred by mental deficiency from ordinary education can be helped to some extent Spastic children she said must first acquire complete relaxation ; then passive movements must be applied later passive active movements must be carried out ; and lastly, active movements

There was much to be done in the field of the infantile cerebral palsies, and neurologically based research should be encouraged

Dr L Massimo (Genoa) read, in translation, the commentary to an English film, previously shown in London This film, entitled *The Rôle of Mental Function in Physical Activity*, was prepared in the cerebral palsy unit at Queen Mary's Hospital for Children, Carshalton, and the associated parents' advice clinic The commentary pointed out that cerebral palsies may occur in mentally normal and in mentally deficient subjects, and that prognoses of ultimate compensation for these non-progressive motor disorders rest on evaluation of the patient's mental function

The film first illustrated the rôle of mental function in ordinary everyday activities of intelligent adults who, having been born without arms, were effectively compensating for their missing limbs The first, a mother of seven children, was shown doing housework and caring for her youngest child, the second, a young man, was shown at work The film then illustrated the development of mental function in normal babies, and showed the defective development of children with abnormalities of brain function Four defective babies were shown during clinical testing for primary abnormalities of mental and motor function. The tests revealed that two of the babies had no motor disorder, and two had both mental and motor limitations These four babies were shown stages of development, and the correctness of the thus demonstrated

The commentary emphasised the need for plann pensatory activity for children with primary motor and demonstrated the results of appropriate pl palsied children shown at play and in school Those of intelligence showed achievements, within their motor appropriate to their ages, and those with mental def failed in this respect Finally, two brothers were normal and one with cerebral palsy The boy with palsy showed activity which closely resembled that brother He had been competently helped from an to use his defective motor function skilfully for expr lively intelligence

The trend of the papers read and the films this congress was towards a new approach to the cerebral palsies—an approach based on neuro logical study of infant development, recognition of abnormalities, and practical application of principles in techniques of diagnosis and of of children with brain deficiencies

Mrs Eirene Collis, C.P T, of the cerebral palsy unit Mary's Hospital for Children, Carshalton, was awar the Italian Republic the *stella della solidarietà italia* services to the children of Italy

# Public Health

## Coloured Food

The Food Standards Committee has adopted a recommendation by its preservatives subcommittee[1] that the Public Health (Preservatives, &c, in Food) Regulations, 1925–53, should be amended so as to permit the inclusion in foods of specified colours only

The subcommittee, whose chairman is Sir Charles Dodds, F R C P, F R S, remarks that the practice of colouring food is by no means new

Pliny the elder, for instance, referred to the colouring of wine But it is only in the past hundred years or so that this practice has been open to possible objection About 1850 the "coal tar" dyes were discovered, and these have now largely replaced the natural colours previously used

In 1924 a departmental committee, appointed by the Minister of Health, recommended that the use of only specified colouring matters, regarded as non injurious to health, should be allowed But the Government of the day decided on a different approach, and under the 1925 regulations the inclusion in food of certain colours then known to be harmful was prohibited These were antimony, arsenic, cadmium, chromium, copper, lead mercury, and zinc, gamboge (a vegetable colouring matter), and five "coal tar" colours (picric acid, victoria yellow, aurine, manchester yellow, and aurantia)

The present position is that the Food and Drugs (Milk, Dairies and Artificial Cream) Act, 1950, prohibits the addition of colouring matter to milk, but otherwise any colours not specifically prohibited by the Public Health (Preservatives, &c in Food) Regulations, 1925–53, may be used in foods, provided that such use does not contravene the provisions of sections 1 and 3 of the Food and Drugs Act, 1938

The subcommittee observes that evidence has been accumulating which indicates that "coal-tar" colours other than the five already prohibited may be a hazard to health in laboratory animals some have proved carcinogenic

Without the addition of colour, says the subcommittee, many foods would have a drab unattractive appearance If, therefore, there is enough evidence that the colours used have no deleterious effect on health, it sees no objection to their being used to replace natural colour l processing, to standardise appearance, or simply a food more attractive But the report suggests that the addition of colour to raw meat, game, po fish, fruit, and vegetables should be prohibited (to best of its knowledge such additions are not being in this country)

The report ends with a list of colours which subcommittee suggests, should be approved for in food

Representations on the subcommittee's recommendations be submitted, up till March 31, to the Joint Secretary Subcommittee, Ministry of Food, Great Westminster Horseferry Road London, S W 1

## Fish and Chip Shops

In his report for 1953, Dr T R Roberton, officer of health for Bootle, describes how his de has been improving the standard of hygiene in chip shops in the borough Generally the shops well maintained, but one possible source of it is certainly not one that is confined to Bootle) improvised shed at the rear of some premises, wh used for storing, cleaning, and peeling the potat which was often an unsuitable place for the job report also refers to the wrapping of fish and ch "an inadequate sheet of grease-proof paper" and newspaper "the source of which was unknown" prietors were recommended to wrap the food in a suitable paper bag and to use "an external wr from an approved source"

## Geography of General Practices

Middlesbrough's health department lately made survey to find out the extent to which the local doctors' practices overlapped geographically report for 1953, Dr E C Downer, medical of health for Middlesbrough, tells how six street selected from different parts of the town, only which some member of the department ha be visiting officially were included in the inquir one street, 18 families were attended by 17 d doctors, in another, 25 families were attended doctors Each street surveyed had 10 or more covering from 12 to 26 families "From this it seen," Dr Downer comments, "that in times of spread illness or epidemics the general practit the town have to motor all over the town to their patients An enormous amount of time be spent by doctors at the wheel rather than bedside, and it is impossible to attach the health visitor as closely to the doctors as one w He suggests that, in the interests of economy, six doctors working in some form of group should be responsible for a large housing e of housing estates,' and that the choice of ors should be limited to those within this group ice

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[1] standards Committee Report on Colouring Matters Stationery Office Pp 27 1s

### Smallpox in France

e French ministry of health states that the port annes in the Morbihan department in Brittany een declared infected with smallpox. Up to Jan 4 ases, including 2 deaths, had occurred Sanitary ures have been applied from that date to departing s.

### Notification of Puerperal Pyrexia

e forms used in notifying puerperal pyrexia are to ltered so that the cause of the disease if known, be stated[1] Regulations to this effect come into ation on March 1, and will apply to all notifications ngland and Wales, including London

### London in 1954

most before the New Year festivities are over, J A Scott and his colleagues in the public health rtment of the London County Council have pub d preliminary vital statistics for the old year London birth rate for 1954 was 15·2 per 1000 lation—the same as in 1953—so the decline which been in progress since 1947 has halted The pro- nal death rate was 10·9 per 1000 population—the st ever recorded The decrease in the number eaths was largely due to a reduction in mortality respiratory diseases. The infant-mortality rate 954 was 22 per 1000 live births, as against 24 in 1953 fications of new cases of tuberculosis in London rom 5078 in 1953 to 4730 in 1954 and there has been rther decline in the death rate from 0·23 per 1000 lation to 0·18—a new low record.

### Third Quarter in Eire

Eire during the *third quarter of 1954*[2] the birth rate 21·0 per 1000 population (0·8 greater than in the quarter of 1953) and the death rate 10·5 compared 0·7 the previous year The infant-mortality rate 30 per 1000 births registered (33 in the corresponding ter of 1953), and the maternal mortality rate was per 1000 (a decrease of 0·4) The death rate from gnant neoplasms was 1·5 per 1000 population as ast 1·4 in the corresponding quarter of 1953 The h rate for all forms of tuberculosis was 0·3 per 1000 for pulmonary tuberculosis) these rates were the as in the corresponding quarter of 1953

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[1] o Puerperal Pyrexia (Amendment) Regulations, 1954 S.I. 1954 no 1691 H M Stationery Office 2*d*.

[2] arterly return of the marriages births and deaths registered uring the September quarter 1954 Government Publications ale Office G.P.O. Arcade Dublin Pp 12 6*d*

### Infectious Diseases in England and Wales

| Disease | Week ended December | | | |
|---|---|---|---|---|
| | 4 | 11 | 18 | 25 |
| heria | 13 | 15 | 18 | 15 |
| ntery | 103 | 357 | 315 | 340 |
| phalitis | | | | |
| ective | | 1 | 1 | 2 |
| tinfectious | 1 | | 1 | |
| poisoning | 183 | 131 | 161 | 138 |
| es excluding rubella | 6017 | 6298 | 6606 | 5540 |
| ococcal infection | 35 | 41 | 31 | 28 |
| almia neonatorum | 37 | 30 | 47 | 27 |
| yphoid fever | 2 | 7 | 6 | 3 |
| nonia primary or influenzal | [illegible] | 768 | 746 | [illegible] |
| yelitis: | | | | |
| alytic | 30 | 30 | 26 | 5 |
| paralytic | 17 | 13 | 10 | 1 |
| eral pyrexia | 233 | 211 | 218 | 179 |
| t fever | 693 | [illegible] | 800 | 673 |
| pox | | | | |
| culosis | | | | |
| piratory | 677 | 723 | 667 | 493 |
| inges and C.N.S | 16 | 5 | 13 | 7 |
| er | 83 | 80 | 1 | 64 |
| hil fever | | 3 | 1 | |
| ping-cough | 2150 | 901 | 1838 | 1956 |

## Before Our Time

# MEDICAL MISSION 1855

M E S LAWS

O.B.E., M.C., F.R.Hist.S

FROM the medical point of view the Crimean War is best remembered for the virtual collapse of the British military administrative system the terrible casualties of Lord Raglan's force from cholera exposure and semi starvation and the failure to provide adequate hospital accommodation staff or equipment Under pressure of public opinion the Government made strenuous efforts to remedy these shortcomings and by early in 1855 there was promise of general improvement But it is not generally known that at this time when our own medical resources were under great strain to provide more doctors *for the army in the Crimea we also made a considerable* and successful effort to help our Turkish ally

Early in 1855 General Cannon who was head of a British military mission with Omar Pasha's army on the Danube reported that the Turkish troops had practically no medical organisation and were losing many men because of this He begged that a British medical staff *should be dispatched as soon as possible* with essential equipment to organise hospital facilities At that time the Government was still recruiting doctors for Lord Raglan's army and was also committed to finding doctors for his Turkish division of 20,000 men and an irregular cavalry corps of 4000 men which were being taken into British pay and service The authorities in London might well have declined to respond to General Cannon's plea and it is to their credit that they accepted this further task

It was decided that the medical mission to Omar Pasha's army should consist of an inspector general of hospitals a deputy inspector general four surgeons (1st class) fifteen surgeons (2nd class) four dispensers twelve dressers a storekeeper and a clerk All except two surgeons and one dresser were British but all were given Turkish military rank, varying from major general to lieutenant As few of the doctors had had any previous military experience it was perhaps inevitable that insufficient stress was laid on the need for physical fitness, and some of those who volunteered proved unable to stand the hardships involved Two surgeons died and the inspector general (Dr J Fuller) two other surgeons and a dispenser were invalided soon after reaching the theatre of war Dr A Farquhar the deputy inspector general then took charge of the mission

*When the mission reached* the Black Sea Omar Pasha had transferred the bulk of his army to the Trebizond district so as to relieve the Russian pressure on Kars The mission therefore moved to the new area: a small detachment was left to organise a field dressing station with the fighting troops while the main body took over the Turkish hospitals at Trebizond and Sinope Conditions in these establishments were chaotic and the records showed a death rate of between 80-90% of admissions The British mission took charge in November 1855 and the following figures cover the seven months they were in control

| *Unit* | *Admitted* | *Died* | *Discharged* | *Remains* |
|---|---|---|---|---|
| Field dressing-station | 111 | 17 | 40* | |
| Trebizond hospitals | [illegible] | [illegible] | [illegible] | 44 |
| Sinope hospitals | 120 | 4 | 116 | |
| Total | [illegible] | 391 | [illegible] | [illegible] |

* Evacuated to hospital

When the mission ended their duties in May 1856 and returned to England the mortality rate had thus fallen from over 80% to under 15% The statistics of this outstanding achievement, which have been taken from Dr Farquhar's official report have never been published but in view of the criticism at that time of the Army Medical Department in particular and of the medical profession in general it would seem only just to place them on record even though they relate to a century ago

# In England Now

### *A Running Commentary by Peripatetic Correspondents*

I'm glad you like the Guidance Clinic,
Sophisticated little cynic,
I'm pleased when you are in a paddy,
It shows you sometimes hate your Daddy
And when you smash up all the lights
It hints at guilty thoughts at nights
You kick my shins and spit at me
Oh *don't* we have a jolly spree ?
But sometimes, sweet delinquent, dear,
You go too far, and then I fear
Your Father figure's gentle smile
Is like that of the crocodile,
Whose overt attitude to fishes
Does not reflect his inner wishes
When cold and tired, with empty belly,
I'd like to beat you, dear, to jelly
*Moral* —Do not put your question to experimental test

* * *

" Many Afghans," a friend from Kabul writes, " are worried, and sometimes caused great pain, by an ailment peculiar to the country, which only their local doctors can diagnose or cure—fallen navel "  If the navel has slipped out of place (that is, is not in correct and equal measurement from the nipples) a specialist is called in to manipulate it back into place  Science and engineering having abolished distance, I feel that cases may, at any moment now, appear in this country  Perhaps we have already overlooked sporadic outbreaks  We should be prepared  I myself am ready with the apt, euphonious, descriptive term " omphalolisthesis "  I am also providing myself with a slightly stretching measuring-tape—made to my own design by Messrs Uppe Bros  Plastic surgery should be on its toes to replace clumsy and painful manipulation by accurate and effective omphalentoporrhaphy or omphalopexy, to be performed under spinal anæsthesia and, of course, in the shade of the indispensible *umbrella penicillinæ*  That 'll show 'em Better fifty years of Europe than a Cycle of Cathay

* * *

The soft airs of the Fortunate Islands are very restful after the rigours of the English winter  From the air the islands spread like mould-eaten bacterial colonies with twisting lagoons, white inlets, and black, ship-tearing rocks

Captain Anson[1] set off from these islands in 1740 with a small fleet of ships only partly crewed with trained seamen  The military complement consisted of five hundred Chelsea pensioners, and two hundred and fifty untrained marines who had not yet been allowed to fire their guns  Less than a tenth of his men survived his trip round the world, and he returned with only one of his fleet of six ships, but with an immense fortune from the treasure ships of Spain  He was full of ideas about the ætiology of the diseases which decimated his crew, particularly the scurvy  Fluxes and tenesmus, he correctly observed, were associated with the filth below decks, and with touching at certain ports  But scurvy was the worst peril, men dying in their tens each day as they rounded Cape Horn and beat their way up to Alexander Selkirk's deserted but beautiful island

The scorbutics bled from their gums and died of obstinate constipation  Their old battle wounds broke down , and in one pensioner a bone healed for fifty years fractured again spontaneously, the callus melting away  The disease carried with it a fatal melancholy—which is not surprising since it was, one feels, more dangerous than shipwreck  Increased danger, or " fatal rumours " caused an increased mortality among the scorbutic  The disease was as severe during the Pacific crossing when fresh fish was eaten daily as it was on the Atlantic voyage on " hard tack "  The patients recovered rapidly after being put ashore, though many died during the transfer from the ships  But patients who had received a boatload of fresh vegetables a week before the weather allowed them to land did not sustain this mortality  This puzzled Anson who was as full of views on scurvy as were [illegible] contemporary literary seafarers  He realised that limes came into it somewhere, but obstinately stuc view that landing on shore was the only true cure he believed, was ill adapted to the foreign element waters, requiring the insensible vapours of terra full health

* * *

My absence from this column has probabl unnoticed by all but myself  Life got me down. has caused my recovery ?  A gadget  No, not a television set but a super-cooker  Any other wife who has spent years trying to keep meals attractive will have experienced my trouble. now press for the cure  My advice to any married is to make sure the wife is happy in the kitchen. domestic chores run smoothly the little woman that she has sufficient vital energy left to cope telephone, the patients and their relatives, the they leave in the hall, and the effect they have husband  She may even find that she has the take up her former hobbies  Look at me—pen again

* * *

The examination for the certificate in public at a school approximately 60 yards from the House of London University began on Dec. 13. Dec 10 the following anonymous notice appeared notice board

*According to a usually well informed member of the following questions are going to be asked at the examination*  Do not try to answer more than at a time !

*Statistics*  1 The Equivalent Average Stan Mortality Comparative Figure for the C P H stu 1795  That for Piano Tuners is 82  What conclus you draw from that ?  (Be frank )

2 What sort of figure is the Registrar General? likely that he will ever be promoted to Field Marsha

*Epidemiology*  In a family with 18 children 1 infected with whooping-cough  Is he (she) likely to

*History*  Write a short note about something that Chadwick did not do

*Public Health*  1 You are the Medical Officer of H of a County Borough  Why ?

2 Make a short comparison between the Rag Flock Other Filling Materials Act, 1951, and the Shellfish (F of Meals) Regulation, 1934

3 " Never before in history have so many learnt so about so much " (C P.H  student)  Discuss this sta

*Genetics*  If a man tells you that his father had p synosotosis, his second cousin was a hæmophiliac, his in law was colour blind, and one of his 7 sons had r pigmentosa, whereas he himself was a schizophrenic, would be your advice ?

* * *

Mother  " I think I shall buy these chocolates I feel in a self-indulgent mood "

Daughter, aged 9  " Surely, mummy, you me embulgement ! "

* * *

## O & M

That O & M's home stamping ground
be carefully protected
each Civil Servant's moved around
ere too much is expected.

Yet you and I can't leave our pitch
to follow their example,
so surgeons will be paid per stitch,
physicians priced per sample

New methods will apply, or should,
(Review teams are quite passé)
and endless belts of plain steam pudd,
will oust the marrons glacés

Sweet secretaries were bad for " firms ",
machines, they say, are better,
for pool typists' medical terms
may brighten up the letter

So, fresh the eye and blank the mind !
Let time checks be abundant !
If Deaths and Discharges drop behind,
some staff must be redundant

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[1] W C  Anson's Voyage Round the World  Harmonds 1948

# Letters to the Editor

## THE MALNOURISHED COMMUNITY

—I write to support Professor Platt s excellent ealistic views (Nov 6) on infant feeding in tech under developed tropical countries

ne rightly says a most important practical approach alnutrition *in this type of community must* be gh the mother and child at the maternity and health centre Unfortunately at present a large rtion of these centres are being rendered valueless lack *of appreciation of the necessity for methods* different from those employed in Europe and North ca To understand this it is necessary to apprec o fact that all pædiatricians and others engaged in ype of work—of whatever nationality—have either trained in the West or have used textbooks written ly on Western style infant feeding When coming ntact with the nutritional problems and feeding ces in the tropics, the pædiatrician with this type of ng is almost always unaware of such aspects of the t as the disadvantages and overwhelming advan of prolonged breast-feeding the scarcity or e (or in some regions the dislike) of animal milk he effect of beneficial and deleterious food pre s Without exception he then passes through a e of bewilderment until he realises that the hed methods learned at medical school are inapplic nder the very different socio-economic and cultural ions found in most of the technically under ped areas of the world Following this two s may be followed—either a cautious attempt to y his teaching in the light of local reality or disas y the adoption of an ivory tower attitude by Western-style instruction on infant feeding nes to be dispensed without either meaning or

correct approach to the teaching of methods of feeding in most under-developed tropical regions at must be remembered, this embraces the majority world's child population) may be envisaged in the ing logical stages

nvestigation of local methods in use in the particular with especial reference to customs, taboos and food ces not only in infant feeding, but also *during* ncy and lactation

*Unprejudiced* analysis of the value or otherwise of methods in their particular cultural and geographical with especial reference to the availability of animal

Teaching of methods of infant feeding based on ole local customs, modified or improved if necessary entific knowledge together with the elimination of il practices. (As an extreme example it may be noted parts of Africa no cattle can be kept at present because tsetse fly In those circumstances where absolutely no milk is available prolonged breast feeding is a bio necessity but can in all probability be improved as he yield is concerned by ensuring that the mother is as d as possible on a diet of locally available foods At me time an undesirable aspect of this practice which be discouraged is the custom of breast feeding an when the mother has become pregnant again )

lly I would like to endorse Professor Platt s tions that the two main initial items in a pro e of infant and maternal care in a malnourished l community are the selection of suitable foods ially vegetable protein foods) for mixed feeding and sign of a diet to enable the mother to lactate ately for two years or even longer These are not ts of interest only to a few anthropologically d pædiatricians but the top problems of infant on in the world today

etta D B JELLIFFE

## MYOCARDIAL TOXOPLASMOSIS

SIR —Dr Paulley and his colleagues reported [1] a series of cases of toxoplasma myocarditis in which the diagnosis was based on serological findings alone In their cases the dye test of Sabin and Feldman and the complement fixation test were both positive both were done as a routine because of the well known non-specificity of the dye test

The interest aroused by this report was shown by the number of sera which were subsequently sent to this laboratory for examination for toxoplasma antibodies from patients with obscure myocarditis In one of these the dye test was positive at 1 32 and the complement fixation test positive at 1 8—findings thought to be diagnostic of toxoplasmosis The patient died a short time later and through the courtesy of Dr Alun Williams I was able to examine a part of the myocardium The well washed and finely ground myocardium was injected intraperitoneally into mice and on the 10th day after primary inoculation abundant toxoplasmas were seen in the mouse peritoneal exudate and passaged from it

This finding emphasises the association between the presence of toxoplasmas in the tissues and of toxoplasma antibodies in the serum and lends weight to the belief based on the serological findings that the cases of myocarditis described by Paulley et al were in fact caused by toxoplasmas

The Hospital for Sick Children
London W C 1

I A B CATHIE

## VENEREOLOGY AND DERMATOLOGY

SIR, When the National Health Service became effective in 1948 venereology was established as an entirely separate and independent specialty a decision which was based upon more than thirty years experience of the venereal diseases scheme and received the approval of almost everyone Since that time there has been a fall in the incidence of first infections with venereal disease an expected development which certainly owes more to peace and full employment and to the efficiency of the service than to new remedies It is clear that some of our administrators are regarding this fall in incidence as an indication that the problem is solved and as an opportunity for saving money Recently a dermatologist was appointed to take over clinics in East Anglia from a venereologist the appointment being advertised under the heading of dermatology although most of the sessions were in venereology

Now comes this advertisement relating to East Kent and Dr Erskine (Jan 8) puts in some special pleading for the suitability of a *combined appointment in thi* area on the rather confusing grounds that (1) there is not enough work to hold the interest of a venereologist in East Kent (2) it is a bad thing to have too much specialisation and (3) a senior registrar in venereology can become competent as a consultant in dermatology by spending part of his time in the dermatological department when working in venereology

Of course it is a good thing for a venereologist to know something about dermatology just as it is a good thing for him to know even more about general medicine cardiology neurology and psychiatry But part time work for three years will not make him an expert in any of these subjects and Dr Erskine s registrar is to be congratulated on his wisdom in not applying for the East Kent appointment

Surely Sir since the principle that the two subjects should be separated has been accepted the appointments in dermatology and venereology in East Kent should be separately advertised and filled by different consultants If as Dr Erskine says there is not enough work for a venereologist in East Kent an area which has large centres of population and important seaports, the explanation may be that clinics are inadequate or badly sited, or that there is not a proper liaison with other departments of the hospitals concerned The late manifestations of venereal disease are commonly to be found among general medical cases and in other special departments If the venereologist has the right degree of interest in his work his colleagues will be anxious to seek his advice and help If, on the other hand, he belongs to some other special subject and has only perfunctory interest in venereology no one will want his advice The result will be a poor standard and a break up of the organisation which has been built up gradually with labour and tears and has produced such excellent results

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[1] Paulley, J W, Jones R Green W P D, Kane J J *Lancet* 1954 ii 621

St Bartholomew's Hospital
London, E C 1

CLAUDE NICOL

## FAILURE OF GLYCYRRHETINIC ACID TO CONTROL ADRENAL INSUFFICIENCY

SIR,—Since Molhuysen et al [1] in 1950 first reported the deoxycortone like activity of liquorice extract, a number of papers have appeared describing the effects of liquorice and liquorice extracts in patients with adrenal insufficiency Several authors [2–7] have described patients with Addison's disease who have been maintained satisfactorily on liquorice extract or glycyrrhetinic acid

In a previous communication [4] we described a patient, a woman of 45 with Addison's disease, whose response to the administration of 50 mg of glycyrrhetinic acid four times daily was in some respects similar to her previous response to deoxycortone injections and cortisone by mouth Eight months after implantation of cortone and testosterone pellets, when these were to be exhausted, a course of treatment was begun glycyrrhetinic acid, 250 mg daily It was hoped it would be possible to maintain her satisfac liquorice derivatives alone, and she received no specific treatment for nine months She re apparently well during this time, but was then a to hospital in a severe addisonian crisis We re alarming experience so that the utmost care may b by others using these preparations in the mana of adrenal insufficiency

In July, 1952, this patient had been admitted to and in September, 1952, she was discharged with 300 mg of deoxycortone acetate and 100 mg of testo She remained tolerably well until May, 1953, by wh the pellets were considered to be exhausted. For the she was given capsules of lactose as a control, and for ten days glycyrrhetinic acid (250 mg daily) was sub As further supplies were temporarily not available, p glycyrrhizinate (500 mg daily) was given instead for th ing four weeks, and this in turn was followed by "dummy" capsules Her condition deteriorated two weeks she again began to take glycyrrhetinic mg three times a day She continued with this following five months, when the dose was increased mg daily Two months later she developed a co three days became drowsy and finally comatose, state she was admitted to hospital

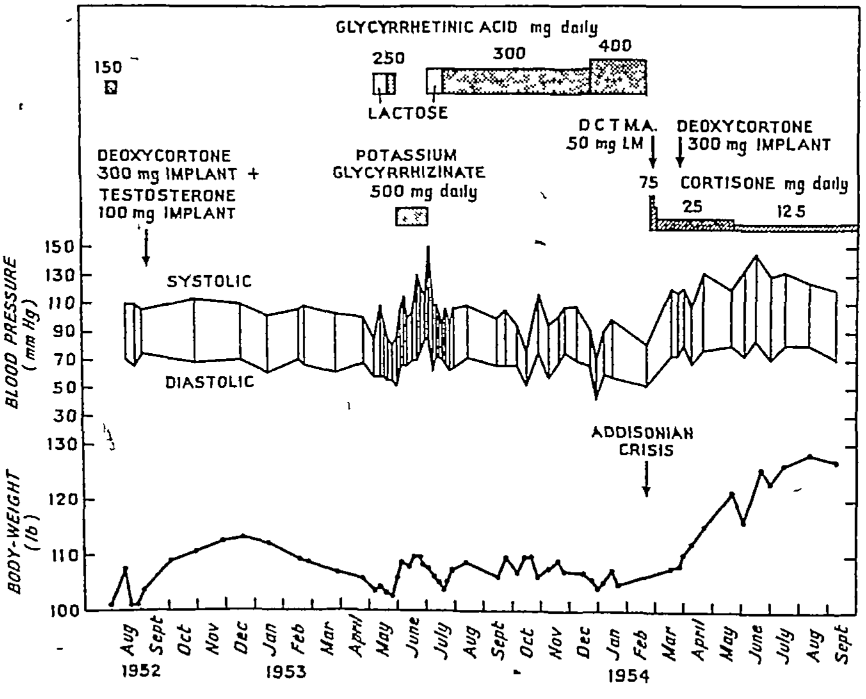
She subsequently claimed that she had taken the of glycyrrhetinic acid up to the day on which she w coma, and her husband confirmed this independently

When admitted to hospital she was deeply cold, cyanosed extremities Axillary temperature was and four hours later 100 3°C Her pulse rate was 110 and blood pressure 90/60 mm Hg Serum sodium centration was 111, serum potassium 3 8, and serum 92 5 m eq per litre, the blood sugar level was 100 ml

She was given intravenous glucose and saline with and intramuscular injections of deoxycortone and acetate Within seven hours her blood pressure had 130/90 mm Hg, she was sufficiently conscious to call use a bedpan, and was complaining of headache. She 1950 ml of urine in the first fifteen hours after admis hospital

Within three days she had recovered and thereafter her gress was most satisfactory has since been maintained implant of three 100 mg p deoxycortone and 6 25 mg isone twice daily by mouth changes in her weight and pressure are shown in the panying figure In her own she "has taken a new lease and has not felt so well for years She is in no doubt general condition on and cortisone is incomparably than while she was taking rhetinic acid, though at the we recorded her statement was "feeling fine

We are satisfied that patient developed acute insufficiency following a time when, as far as ascertained, she was dose of glycyrrhetinic which she had been ma in health for several mon was remarkable that, she had had no diarrhœa apparently vomited only her serum sodium concen had fallen as low as 111 per litre while at the



weight and blood pressure in response to various forms of treatment (D C T M A = microcrystalline suspension of deoxycortone trimethylacetate)

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1 Molhuysen J A Gerbrandy J Vries, L A, Jong J C Lenstra J B, Turner, K P, Borst J G G *Lancet*, 1950, ii, 381
2 Groen J Pelser H E Frenkel M. Kamminga, C E Willebrands A F *J clin Invest* 1952, 31 87
3 Groen J, Pelser H E Willebrands, A F Kamminga, C E *New Engl J Med* 1950 **244** 471
4 Card W I Mitchell, W, Strong J A Taylor N. R. W, Tompsett, S L, Wilson J M G *Lancet* 1953 i 663
5 Parish, A E, Alpert L K *Amer J Med* 1953 14 522
6 Pelser H E Willebrands A F Frenkel, M, Van der Heide R. M Groen J *Metabolism* 1953 2, 322
7 Calvert, R. J *Lancet*, 1954, i, 805

erum potassium concentration was also depressed 3 m eq per litre and later fell as low as 2 4 m eq tre. We attribute the initial low serum potassium ntration in this patient with Addison's disease ie glycyrrhetinic acid, but this deoxycortone like conflicts with its failure to prevent the serum m from falling to the unusually low figure of n eq per litre. A similar paradox was noted by h and Alpert [4] in one patient treated with syrup quorice who showed increased potassium excretion alternate positive and negative sodium balance.

view of the patient's subsequent progress it is that when she was having glycyrrhetinic acid her ition was much less satisfactory than when later vas given deoxycortone and cortisone. It is unwise neralise on experience with one patient but we that glycyrrhetinic acid alone is not a suitable itute for conventional treatment in more severe of Addison's disease. We do not suggest that rrhetinic acid or crude liquorice preparations are pharmacologically active but rather that for some nts they may be inadequate as the sole form of ment, much as deoxycortone alone is inadequate he proper maintenance of patients with adrenal ficiency. Neither deoxycortone nor glycyrrhetinic has any appreciable effect on carbohydrate meta m and cortisone or hydrocortisone is required to ct this deficiency. Molhuysen et al [1] and Borst [2] found that some patients with Addison's disease l to respond to treatment with liquorice derivatives. t is possible that with the development of the disease atient had become unresponsive to the drug.

rst et al [3] have described a synergism between rrhetinic acid and cortisone, though Hart and urd [5] were unable to confirm this. We wonder fore whether those patients with adrenal insufficiency have apparently been satisfactorily maintained for periods on glycyrrhetinic acid may not in fact have secreting small amounts of adrenal cortical hormone without the addition of glycyrrhetinic acid l have been insufficient to prevent symptoms of al insufficiency. There is of course the possibility our patient had neglected to take the drug; or atively that if the dose had been considerably r she might not have developed an addisonian

are grateful to Dr Wm. Mitchell of Messrs. Stafford & Co., Ltd for supplies of the liquorice derivatives used.

J A. STRONG
J M. G WILSON

dern General Hospital
Edinburgh.

## FLUOROACETATE POISONING

t.—As you say in your annotation of Dec 18 on control of rats and mice sodium monofluoroacetate ngerous to mammals. Yet if properly handled by ed personnel it can perform its function and do no to man or domestic animals. This anyhow is the rience of one group of commercial specialists over years, during which there has been no evidence of ity to the operators or to animals other than rats mice.

tterly we have been working on a derivative of sodium acetate fluoroacetamide which tested pharmacologically ts and mice proves to have an L.D$_{50}$ about twice that of m fluoroacetate (about 4 mg per kg for the amide g per kg for the sodium salt) and moreover to produce mild symptoms of toxicity and none of the epileptiform lsions characteristic of sodium fluoroacetate poisoning. his reason fluoroacetamide has now been suggested as a rodenticide in place of sodium fluoroacetate and details hortly be published. Although its toxicity is less than of the sodium salt it is, it appears quite sufficient to it an effective rodenticide.

It is now well established by the work of Sir Rudolph Peters [1] that the toxicity of sodium fluoroacetate is due to formation in vivo of fluorocitric acid and it is our suggestion that fluoroacetamide is only slowly converted into this toxin as compared with sodium fluoroacetate thus giving only small blood-concentrations of fluorocitrate (sufficient to kill rodents but not sufficient to cause violent death) and a larger margin of safety in use. It is of course to be hoped that antidotes to fluoroacetate poisoning will continue to be sought; fluoroacetamide may be more likely to yield to treatment than sodium fluoroacetate in view of the probably lower blood concentrations of fluorocitrate when amide is used.

It is well known that the higher mammals are less susceptible to fluoroacetate poisoning than are rodents. Professor Adrian has taken a dose of sodium fluoroacetate sufficient to produce a urine toxic to guineapigs. For monkeys the L.D$_{50}$ is about 15 mg per kg.

Recently Saunders and Hughes [2] have shown that enzyme degradation of a C–F bond is possible; this, too leads us to a more optimistic view about the possibility of antidotes to fluoroacetamide and fluoroacetate poisoning.

M A PHILLIPS
Consulting Chemist

Romford Essex

## HEAT TO THE HEART

SIR,—Some eighteen months ago I discovered that heat applied to the cardiac area very quickly relieved an attack of angina and if applied sufficiently soon it would completely abort it. The means used were either an electric pad (the smaller the better) such as are sold for use in bed or a face cloth or handkerchief wrung out in very hot water. The latter method is quicker but requires frequent renewals and the handkerchief must be 110 F on application to be effective (just a little hotter than can comfortably be tolerated on one's own bare arm—not by a nurse's hand). The handkerchief may be used while the electric pad is heating up. The relief obtained is augmented by sips of hot water or hot tea. The pain is relieved much more quickly though perhaps not more certainly than by glyceryl trinitrate and the method is more reassuring to the patient and may be preferable. In some circumstances it may be the only one available (even if the patient is out in a car a handkerchief can be dipped in the radiator or hot water obtained from a nearby house).

There is also no doubt that cold can precipitate an attack. That there may be a fundamental principle involved is now suggested by the work of Andjus at Belgrade confirmed by Smith et al and quoted in your survey on experimental deep hypothermia.[3] Andjus found that in extreme hypothermia cardiac arrest in animals occurred at 0°C and that by warming the whole body plus artificial respiration the animals could not be revived; and they all died. He then discovered however that if heat were first applied *locally* to the cardiac area (for example by putting a heated metal object on the skin) and if this was combined with artificial respiration the heart began to beat again and the animals recovered. Thus the risk of anoxia of tissues (including the brain) during re warming could be avoided. That is to say keep the general metabolism of the animal (patient) as low as possible supply oxygen and stimulate *only* metabolism of the heart and spontaneous revival becomes possible.

Angina may be regarded as a threatened cardiac arrest and cardiac arrest may be induced by hypothermic and hypotensive drugs. In any of these threatened emergencies it would therefore seem logical to apply heat *locally* to the cardiac area as a first step accompanied by full use of oxygen and perhaps cooling of the head by ice-cold water in order to reduce cerebral metabolism, and so perhaps avoid the cerebral sequelæ that may follow recovery. People are more right than they wot of when they say there was a struggle between his heart and his head. There is always intense competition in the last resort between the two for glucose and oxygen and if the heart is in extremis it is surely desirable to lessen this competition, and give the cardiac muscle a favourable balance for a few minutes.

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rst J G G ten Holt S P Molhuysen, J A Vries L A bid 1953 i 657
rt I D Leonard J C Ibid 19 i 801

1 *Endeavour* July 1954 p 14
2 Saunders B C, Hughes G M K *Chem & Ind (Rev)* Sept 9 1954 p 1063
3 *Lancet* 1954 ii 4 9

Whether the method would be of use in cardiac arrest associated with drowning and electric shock is an interesting speculation, and it is being tried in this country Trained first aid surf teams have noted that the colder the water the more difficult it is to revive the drowned person by any of the usual methods Here the layman on the beach and the scientist in his laboratory seemed to have arrived at similar conclusions

Wellington New Zealand H P PICKERILL

## MERIT AWARDS

SIR —Dr Fletcher urges that moneys voted by Parliament for the National Health Service should be used to subsidise research other than that covered by the statute of 1946 as amended I am not belittling research when I say that I believe the proper course would be for Parliament to be asked to increase the present grants for research if it be deemed desirable to increase the emoluments of research workers I consider that the diversion of public funds is the issue

I think Dr Fletcher is wrong in supposing that the merit awards were instituted as a compensation for lost private practice

Sheffield 11 ARTHUR JORDAN

## TUBERCULOSIS IN IMMIGRANTS

SIR,—As far as the Island of Lewis is concerned the paper by Dr Hess and Dr Macdonald [1] was an excellent appraisal of the position as it was 100 years ago, and as it could be in a very few years, but not as it has been from the beginning of this century till now My experience confirms their views and that of others that the Celt is no more prone than other races to tuberculosis, but rather the high incidence and mortality spring from social factors almost entirely—at least in Lewis

The Registrar General informs me that mortality figures for Lewis begin in 1871 Comparative rates for that year are Lewis 92, Glasgow 668, Scotland 398, Orkney 150, Zetland 171 By 1914 Lewis was up to 310, and it ran at a higher rate than Glasgow from 1912 till 1936 Housing in Lewis began to improve in 1930 and the rate fell till 1942, when it was down to 50 but it rose yearly to 162 in 1948 It is still higher than Glasgow, the 1953 rates being Lewis 76 and Glasgow 43

My view that the position from 1900 to 1954 is different is based on the following data

(1) In 1942, when I was in charge of the local sanatorium, youths of 17 who volunteered for work of national importance came to me for examination X ray examination showed that more than a third had tuberculosis, which in many cases necessitated sanatorium treatment The youths called to H M Forces did not have an X ray examination Many returned after a few months' service, discharged because of tuberculosis Had they had an X ray examination on call up they would never have been accepted Of 225 deaths since 1940, 64 were in Service personnel

(2) In 1949 a tuberculin sensitivity survey carried out among all school children (4000) and in youth clubs, factories, offices, shops, &c , yielded very high positivity rates 5–6 years, 18% , 5–12, 26% , 15–20 69% , 21–25 81% , 26–30, 91% , 30 +, 96%

(3) In every case of tuberculosis since 1950 in a Lewis person who has left the island, I have a record of a positive reaction before they left home

Thus I believe that the islander develops an already existing focus which breaks down under studies or work, rather than that he contracts the disease for the first time in the cities Contrast the following positivity rates after a re survey of school children in 1954 5–6 years, 2 7% , 5–12, 14% It may be thought, as I myself believed in 1949, that my positive reactor rate was exaggerated, but now I am convinced that the results substantially true because, in the case of school- en, I had several hundreds examined radiologically e regional hospital board and many of the children showing definite evidence of intrathoracic tuber have now reverted to negative reactors Further, i case of those over 15 the tests were all intradermal 10, and 100 T U ) and the vast majority reacted to 1

This is why I say that the situation could, in years, become what it is commonly held to be vaccination, I may add, was offered and given to of any age who was negative to 100 T U foll 1949 survey

Stornoway
Isle of Lewis R STEVENSON D

SIR,—When the B C G schemes are fully devel Ireland the problem of the tuberculin negative emigrant in Britain should be largely solved and anxiety at present felt by chest physicians, b Ireland and Britain, allayed Varying degrees of p have been made up to the present Some co have only just begun B C G vaccination, but in others progress is well advanced In Tipperary (N Riding) priority has from the beginning, 1950, given to testing and vaccinating contacts, adole and young adults Vaccination was offered to all be the ages of 14 and 30 years in 1951–52 School-le have been done each year since that time. 65% of estimated total of adolescents between 15 and 19 then dealt with, but the response from those bet 20 and 30 was poor, the average being not much l than 30% However, with the addition each ye school leavers to the general pool a respectable t being built up for the last two years, 85% of t leavers have been vaccinated

It is yet too early, of course, to report results, b figures of new cases of pulmonary tuberculosis occ 1954 are beginning to show a very favourable pictur I believe is due to the vaccination The proportion cases in people between 14 and 29 years, which was 1951, and in the two following years 51% and 4 dropped this year to 38% At the other end, the pro of new cases in those over 40 has risen from 27% to 4 1950 8 new patients were returned from England, e treatment or convalescence In the following ye numbers have fallen to 5, 5, 3, and only 1 in 1954. statistics show some improvement at least in the which obtained four years ago, and I believe that next two or three years there will be greater improve

There are at present two unknown factors which my optimism One is that the youngest age for em from this country is from 17 to 19 years of age vaccination done at 13 in a rural district protect un age when the occurrence of a natural infection in the vening years is not likely? Secondly, we are at using in this country two prevaccinal tests, with 1 in 5 1 in 100 old tuberculin An unknown number of reacting to the 1 in 100 dilution are still susceptible to t losis Already in this county, with our small num cases of primary pleurisy with effusion and a primary c have occurred in young persons who have been rec being positive to 1 in 100 There is no doubt but that future, the strength of the last prevaccinal test will ha cut down

The figure of 14 5% positive at the age of 18, r Flynn and Joyce,[1] should not be taken as general Ireland The figures for Tipperary (N R ) are 10% (2145) , 15, 44% (600) , 18, 55% (400) , 22, 63 25, 70% (227)

From the age of 15 to 24 years the propo females was, on average, 5% less than that for Over that age the figures were nearly equal though the size of the average Irish country t only between 1000 and 6000, there is a striking di between the infectivity-rate in the urban an rural portions of the country In the rural po this county, 41% between 15 and 19, and 53% b 20 and 24, are tuberculin-positive In the to corresponding figures are 72% and 82%

Public Health Offices,
Nenagh Tipperary J B O'B

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[1] Hess F V, Macdonald N Lancet, 1954 ii 132

[1] Flynn, M P, Joyce, J C Tubercle, 1954, 35,

## BED WEIGHING MACHINE

—Dr Flear (Jan 8) and Dr Darmady[1] have not oned the possibility of error in estimating the varia in weight of a patient due to alteration in the ure content of the bed clothes An error due to this be significant Through the courtesy of the burns at the Birmingham Accident Hospital I was able e the Avery weighing machine for the following lment

nattress with bed-clothes and linen were exposed to the d November atmosphere in an unheated part of the al A bed was then made up and heated by an artificial (a steel cylinder of approximately the same surface s the body) and heated by two light bulbs to a tempera f about 100 F between the cylinder and the mattress ed was kept in a room at a temperature of 78 F for eight hours. The mattress alone lost $15^1/_4$ oz the ess and bed-clothes together lost 31 oz.

ese conditions are of course entirely artificial the opposite is more likely to occur in practice resses and bed linen are put into use after being ughly aired and they may fairly quickly pick up ure from the atmosphere or from the patient practical way to overcome this difficulty is to use a ress such as a Dunlopillo, which did not alter eight in a similar experiment, and to remove as n as possible in the way of blankets and linen from ed each time the patient is weighed

y Oak Hospital,
mingham, 29

W M PHILIP

## HEARING TESTS

—While agreeing with most of Professor Ewing's rks in his statement published in your issue of 1 on sweep frequency screening tests of hearing ms desirable to point out that partial deafness of everity necessitating special educational treatment d be detected before the age of five years if it is of nital origin Such deafness should be detected ably before the age of one to two years so that the may receive auditory training during the period of al physiological speech development If acquired ess should occur rehabilitation should start straight as soon as the child is well enough.

vould be unfortunate if the impression were given t is satisfactory to defer tests of hearing until the o group tests are done at the age of five The for deafness at an earlier age is long overdue postnatal clinic would seem an ideal place for sing the mother's awareness of the possibility nplications of partial deafness

on, W 1

EDITH WHETNALL.

## REPAIR OF FEMORAL HERNIA

—May I add my testimony to that of Mr Pearce 3)[1] For some years I have also used the supra extraperitoneal approach for femoral hernia[2] o[3] having cited this and seven other perabdominal ls, dismisses them as ' not in general use nd it rapid easy and satisfactory

method is similar to that described by Mr Pearce that it is preferred to reveal the extraperitoneal by divaricating the recti and pyramidales through a ddline incision slightly overlapping the pubis. It is ant to avoid the branches of the epigastric and obtura ble by mobilising the sac posteriorly then laterally and anteriorly It is usually delivered from the canal e and may be ligated and dislocated so as to present peritoneum at the femoral ring Like Mr Pearce I nd repair unnecessary and I hope to produce statis lence for this shortly On one occasion it was necessary into a hæmatoma in the infra inguinal fold, and I opportunity to inspect the ring which had closed ously in a few days.

If the hernia is strangulated the neck of the sac must be controlled with clamp or finger to prevent the sanguineous exudate from entering the general peritoneum. If gut resection is necessary (and that is rare) it may be done with ease without extra incision

Ill effects are rare I have had one hæmatoma and one midline hernia, which was in a very old man I have seen a patient with a good result two years after a septic dehiscence of the wound The operation needs a relaxing anæsthetic and is not very suitable for local infiltration. It is better avoided if one is not sure whether the lump may be an inflamed gland It is rather messy in fat patients with old and adherent hernias, but so are most methods.

The main advantages are the ease with which the sac can be excised and high ligated and the stump dislocated and the opportunity clearly to inspect the femoral ring bladder great vessels and if necessary peritoneal contents The approach gives access to all inguinal femoral and obturator orifices I use it for closing the ring of sacular direct inguinal hernias with a nylon gauze prosthesis. It is however hardly worth doing for oblique inguinal hernias unless at the same time as other retropubic operations

Hull

J CLAPHAM COATES

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Darmady E M *Lancet* 1954 ii 689
Henry A K *Ibid* 1936 i 531
Watson L F Hernia London 1948 p 314

## OPERATIONS ON THE HEART

SIR —I must take serious issue with you over your leader of Dec 25 You state that Wilson et al have identified two fundamental types of electrolyte pattern in the cardiac patient the reference being to a paper published in 1954 The existence of hyponatræmic states in patients with cardiac disease has been known for at least six years and a great deal of work has gone into explaining the mechanism of this development most of which bears little relationship to your subsequent discussion

You begin by stating arguments that hyponatræmia represents sodium depletion brought about by a salt restricted diet and on this basis advocate intravenous hypertonic saline But further on we are told that commonly the total exchangeable sodium value is high The question of sodium depletion in these patients cannot be settled by the value of serum sodium alone but must be determined by balance studies and/or muscle biopsy analysis. Depending on how great the hyponatræmia is how much œdema (or extracellular sodium) the patient has and how much sodium has been transferred into cells these patients may be either sodium depleted or have a total excess of sodium in their body fluids as a whole

This is however only a side issue in the electrolyte physiology of hyponatræmia for the studies of Squires et al[1] and Cort and Matthews[2] have shown that such patients have an intracellular potassium deficiency which is partly replaced by an increase in intracellular sodium and water The serum sodium level represents not the state of body sodium stores but the state of extracellular osmotic pressure, which in turn reflects changes in intracellular osmotic pressure If serum sodium concentration is low it reflects a lowering of intracellular osmotic pressure or a disturbance of forces within the cell maintaining extracellular osmotic pressure These patients are indeed ill but it is changes in intra cellular osmotic pressure sodium content and pH that threaten them not the state of body sodium stores The administration of hypertonic saline to patients who have hyponatræmia with potassium deficiency may raise serum-sodium levels for a short time but will soon lead to little more than a further increase in œdema fluid If such patients respond to anything clinically or biochemically it is to prolonged administration of both potassium and protein since both are needed to replace depleted states of the intracellular fluid My own experience now includes the successful treatment of 25 hyponatræmic cardiac patients with extracellular hyponatræmia, hypochloræmia, and alkalosis by this therapy, while the administration of hypertonic saline has led to everything from pulmonary œdema to a tremendous thirst (with water by mouth these patients immediately dilute themselves back to their initial low serum sodium level) Hypertonic saline has led to everything, that is, except a lasting improvement in the patient's bio chemistry The recent demonstration of the relationship of potassium metabolism to the therapeutic action of digitalis only further underlines the importance of metabolic preparation of patients for cardiac surgery, but it must be a detailed and careful analysis

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[1] Squires R D Singer R B Moffitt G R jun., Elkinton J R *Circulation* 1951 4, 697 Squires R D Crosley A P jun Elkinton, J R *Ibid* p 86
[2] Cort J H Matthews H L *Lancet* 1954 ii 1202

Institute for Cardiovascular Diseases,
Prague
JOSEPH H CORT

## A BLOOD-TRANSFUSION PUMP

SIR,—I was interested to read in your issue of Nov 13 a description of a transfusion pump by Mr Martin I can confirm his remarks regarding the value of rapid intravenous transfusion, which appears to be as efficacious as the inter-arterial route [1]

I have been using a transfusion pump with the same features as that devised by Mr Martin for the last five years It was described in the *British Medical Journal* in 1953,[2] and has been manufactured for the last two years by the Bax Engineering Co, Wheatley, Oxfordshire I may add that the principle of the flexible tube compression pump has been known for over fifty years, the main difference between the older models and those described by Mr Martin and myself being the inclusion of a method of adjustment of the pump for different tube diameters This improvement avoids the necessity of using special tubing and opening of a transfusion line

University College of the West Indies
St Andrew Jamaica
V J KEATING

## DISTRIBUTION OF CHRISTMAS GIFTS

SIR,—I am sure that your readers will be pleased to learn that the contributions to provide Christmas gifts for the beneficiaries of the Royal Medical Benevolent Fund amounted to £2775 We were able to distribute £8 to each of them

The warmth of gratitude expressed in letters of thanks would have gladdened the hearts of the contributors

WEBB JOHNSON
President
London, S W 15
Royal Medical Benevolent Fund

## THE LABORATORY TECHNOLOGIST

SIR,—As medical laboratory technologists we feel that Dr Davey's article of Dec 11 cannot be allowed to go unchallenged

We feel that the present-day technologist has sufficient understanding of the techniques available to him to make an intelligent appraisal of them and that he therefore will not take the short cuts Dr Davey mentions It is only in those laboratories in which a thorough training (theory as well as practice) is not provided that the situation he describes can arise Furthermore, technologists are not in the habit of taking unfair advantages of their medical associates We are not such a Machiavellian band

The present-day entrant to medical laboratory technology is, and should be, an intelligent person, and he is as capable of reliable and honest work as a medically qualified person If this were more generally understood and accepted, relations between the clinical pathologist and technologist would be easier It is the seeming lack of mutual trust that is driving away the more suitable entrants into other fields

Professor Bedson, in an address to the London branch of the Institute of Medical Laboratory Technology, spoke of the increasing difficulty in finding suitable male entrants He suggested that an increase in salaries would overcome this problem Such an increase would certainly be appreciated, but there are those who fe improvement in status would be of greater val

Dr Davey's article certainly does not help to the problem of recruitment

A. W P
Aldershot Hants
PETER

## THROMBOPHLEBITIS FOLLOWING INTRAVENOUS INFUSIONS

SIR,—Mr Jones's experience (Nov 6) must b shared by most of us in greater or lesser degree time to time attempts are made to incriminate factor, and the current favourite appears to b phurous compound in the red rubber of the giving set There are so many variables in this f only by pooling knowledge can definite concl reached My object in reporting my own (ad incomplete) investigations is to stimulate spread inquiry

The general aim should be to eliminate ea factor in turn by studying large numbers of co infusions The factor investigated in my own was red rubber I first studied 79 infusions in 46 p using the standard Regional Blood Transfusion drip sets, a similar study was then made of inf which plastic tubing had been substituted for r

A robust dripper was made by Mr Watts, of Ham Hospital technical staff, who modified a 'Plim that the sizes of 'Polythene' tubing then availab would fit the lower end Mr Watts also made metal adaptors to connect the polythene tube to needles The apparatus was unpopular in the theatr the anæsthetist was unable to use it for intravenous so a two way tap was added to the needle in the t removed before returning the patient to the war

Cold polythene does not compress easily, so th was controlled by altering the height of the bott infusion is not possible with the smaller sizes of p but I understand that larger sizes are now availab

Only 10 infusions were given with polythe but the fact that such drips were not entirely fre suggests that something other than rubber is the ca problem On the other hand, in 5 of the 10, there reactions, in 5 there was only simple thrombo reaction), and in none was there any pain, re tenderness (moderate and severe reactions) The f the rubber series were 15 (19%) with no reaction l with mild reactions, and 47 (60%) with moderate reactions

The results once again emphasise that infusion eight hours' duration are the ones likely to give

Of the 15 rubber tubing infusions without reactio lasted more than eight hours, and of the 5 plastic infusions without reactions 3 lasted less than eight lasted nine hours, and 1 lasted twenty four hours T is not the complete answer is shown by the 14 ca reactions after infusions lasting eight hours or les case the reaction was severe Of the 17 cases w reactions after rubber tubing infusions, 13 had had of ten hours or less, whereas in none of the 5 cases w reactions after plastic tubing infusions had the infus less than ten hours These results show that infusions through rubber tubing are more danger prolonged transfusions through plastic tubing

It was impossible to say whether the type of flu influenced the incidence of thrombosis, since the transfusions were usually of short duration w dextrose or saline infusions were more prolonged was no apparent association between the type o or length of operation and drip thrombosis. Mo half the patients were between the ages of fi eighty there was no obvious connection severity of reaction and age In 12 cases it is that a mask was worn while setting up the drip of these had no reaction 11 transfusions were in the theatre and only 1 of these (a two hour was trouble free Records of dressings applied re site are incomplete but it is certain that some with no dressing had no reaction and some with ito sterilisation had severe reactions There seems loubt that the reaction is not an infective process. 3 cases cannulæ were used on forearms, and 3 ped severe reactions In 4 cases cannulæ were used les, and in all severe reactions developed support ie common belief that reactions in the leg are oner and more severe than those in the arm of the leg infusions lasted less than twenty hours imber of severe reactions with cut-down trans s was much higher than with simple needling and innot be explained satisfactorily by the time factor ie the number of needle drips running for twenty or more without more than a moderate reaction most a third of the total

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[1] Gardner O C Keating V J *Anæsthesia* (in the press)

[2] *Brit med J* 1953, i, 94

ve prepared a table giving full details of each patient will gladly supply a copy to any of your readers who e interested.

o studies were made in the surgical wards of one small ree large London hospitals but the initial work was t the Postgraduate Medical School of London. It is sure to acknowledge the encouragement and help of edical nursing and technical staffs of the school and spitals.

ock Hospital,
bury Wilts

J Morris

## TERATOMATOUS NÆVI

—According to my definition of all that I would y under nævi and nævoid structures[1] I would e some abnormalities which I now think are really atomatous nature—for example what I termed ipoma of the pituitary body long ago[2] I venture o because I believe it is an important consideration structures may contain embryonic remnants, ially capable of producing malignant tumours, as chorion carcinoma (compare my note[3] on e and female teratomata)

on N W 1

F Parkes Weber

## SANATORIA

—In tuberculosis as in all diseases, we have to pecific as well as constitutional methods of treat —the first indicated by the disease the latter ed to the psychophysical personality of the patient the object of raising his resistance The specific ds of treatment (antibiotics, chemotherapy and y) are the greatest help but they cannot alone ce a complete cure and constitutional methods always be the centre of our endeavours.

stitutional methods cannot however be vaguely sed as mental rest pure air adequate nutrition. t work on metabolism endocrinology neuro ative physiology and medical psychology allows more precise knowledge of the human constitution ius for a more accurate picture of the constitutional s of each particular patient This makes for a more al application of dietotherapy climatotherapy otherapy and of certain constitutional pharma al agents The sanatoria are institutions where onstitutional procedures are applied and they have ihtedly rendered great service

s fact that sanatorium treatment has often been d on wrong psychological lines—as that novelist dius Thomas Mann showed in his *Magic Mountain* s not mean that such treatment should be aban Sanatoria will always be useful but their methods to be modified because whereas even a few years inatorium treatment was everything in tuber s treatment today it is only one factor in a complete therapeutic constellation and in sanatorium treatment the new knowledge of constitution should be taken into consideration.

London W 1

A P Cawadias

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[1] ces Weber F On Nævi and Miscellaneous Subject London 6* p 7

[2] ces Weber F Dawe 1 *Trans path Soc Lond* 1907 58, p D

[3] *Ir* 1954 237 550

## CANCER OF THE LUNG

Sir,—The absence of any mention of a relationship between cigarette smoking and lung cancer by the chief medical officer of the Ministry of Health in his annual report is certainly difficult to understand Although most members of the public have now heard of this connection it is surely time that more authoritative advice was given to them and the same kind of effort and initiative which was put into the successful campaign against diphtheria should now be directed against lung cancer Although other factors may be important few can seriously doubt that cigarette smoking is the most important

Apart from the work of Bradford Hill and Doll Hammond and Horn[1] have produced convincing evidence from the United States In a study of 187 766 white males between the ages of 50 and 69 they found that the death rate in all smokers was 52% higher and amongst heavy smokers 75% higher than in those who had never smoked The higher death rate in the smokers was largely due to cancer of the lung and coronary disease Such evidence emphasises the need for the widest education of the public on this subject

London W 5

Keith Ball

## ENDOCARDIAL FIBROSIS

Sir,—I was interested to read Dr Still s article of Dec 18 I suggest that this condition should have been called endocardial fibro elastosis a the prominent feature is the presence of generalised endocardial thickening with proliferation of both collagenous and elastic tissues In adults mural thrombi with resultant emboli can occur The myocardium is usually normal though patchy myocardial fibrosis is sometimes also present

This condition should not be confused with endomyocardial fibrosis found in East and West Africans Endocardial fibro-elastosis in infancy is associated with other congenital anomalies—i e., hypoplasia of the aorta bicuspid aortic valves coarctation, patent ductus and aortic and mitral stenosis due to involvement of the endocardium of the valves by the same process. Some of these were also present in Dr Still s cases. *There is a family history of congenital heart-disease in* 20% of those cases[2]

Gowing[3] mentions that most affected children died in the first year of life though Dr Still says that sudden death due to this cause in infancy is not widely recognised in this country I should like to point out that this condition can also occur in other age groups. White and Fennell[4] described two cases in men aged 71 and 50 both of whom suffered from angina pectoris and eventually died of congestive heart failure Thomas et al[5] have described 20 cases with necropsy reports and have arbitrarily divided endocardial fibro-elastosis into three groups—infantile (under 2 years) childhood (between 2 and 16) and adult (over 16) The hearts in all of the cases in this condition are usually enlarged and the electrocardiograms show various arrhythmias heart blocks and ST changes The clinical picture may also vary in different cases

Although as Dr Still points out the ætiology is unknown Johnson[2] has put forward an interesting suggestion that endocardial fibro-elastosis results from anoxia of the endocardium due to premature closure of the foramen primum or foramen ovale at an important stage of intra uterine life This condition has also been discovered in stillborn infants

Victoria Hospital
Blackpool

Hari Vaishnava

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[1] Hammond E C Horn D *J Amer med Ass* 1954 155 1316

[2] Johnson, F R *Pediat Clin N Amer* February 1954

[3] Gowing N F C *J Path Bact* 1953 65 13

[4] White P D, Fennell R H Jun *Ann intern Med* 1954 41 333

[5] Thomas W A Randall, R V, Bland E F, Castleman B *New Engl J Med* 1954 251 327

## LYMPHŒDEMA PRÆCOX

SIR,—Having read your annotation of Jan 1, we would like to draw attention to a recent publication[1] by ourselves on the treatment of this condition Although the decision to operate must remain an individual one, it should no longer be necessary to reserve radical excision for the huge leg Size alone is an inadequate criterion of operability, and other factors, particularly the recurrence of acute erysipeloid attacks, are of equal importance

The technique which we have described allows the whole of the subcutaneous tissues of the lower leg and the dorsum of the foot to be excised and grafted at one operation lasting just over one hour During the excision, bleeding is prevented by using a pneumatic cuff tourniquet and neither hæmorrhage nor shock has been a feature It is therefore justifiable to offer operation to patients with relatively mild degrees of lymphœdema

Plastic Surgery and
Maxillo facial Unit
Glasgow Royal Infirmary

THOMAS GIBSON
J SCOTT TOUGH

## ARTIFICIAL HIBERNATION IN POLIOMYELITIS

SIR,—In the Brunswick epidemic of poliomyelitis in 1952 62 early cases were treated with continuous sedation, using the barbiturate 'Somnifaine'[2] Paralysis developed less frequently, and was less extensive, than in a control group of patients who did not receive the drug

In view of this I suggest that it would be worth while investigating the effect on poliomyelitis of artificial hibernation, since each constituent of the "lytic cocktail" has a relevant pharmacological action During the phase of "minor illness," and in the preparalytic stage, chlorpromazine and promethazine would sedate the patient and rest the motor neurones, without endangering the brain-stem centres Chlorpromazine relieves pain and induces a feeling of euphoria—both beneficial effects in the paralytic stage of the disease, especially when the patient has to have artificial respiration In bulbar respiratory paralysis chlorpromazine would, by lowering the basal metabolic rate, decrease oxygen consumption and so lessen the risk of anoxæmia The analgesic effect of both chlorpromazine and diethazine would reduce respiratory pain and allow deeper and more regular respiration, and by their atropine like action chlorpromazine and thiazinamium ('Multergan') would diminish the mucous secretions in the respiratory tract

Brunswick Germany

TH BREHME

## "TAKE A COUPLE OF FAT VIPERS"

SIR,—With reference to Francis Steer's observations on viper wine, the therapeutic administration of the viper dates from antiquity, it was used by the Emperor Nero's physician and its virtues were extolled by Galen

Dr Lyonnet[3] tells of a letter written in 1675 by a French noblewoman which included a recipe for the preparation of a soup made from vipers Fat of the viper was claimed to have aphrodisiac properties, and its dried liver was said to stimulate contractions of the uterus Preparations including the viper as a constituent were still contained in the French Codex of 1908 The medicinal value of the viper has not as yet been substantiated, but it seems unlikely that any modern physician would deem it necessary to undertake a therapeutic trial

The Royal Free Hospital
North Western Branch
Hampstead London N W 3

F CLIFFORD ROSE

SIR—Those who are attracted by Mr Steer's suggestion to "take a couple of fat vipers" may be interested in the following recipes taken from *The Dispensatory of the Royal College of Physicians, London* (1746)

JUS VIPERINUM

Take a viper of a middle size without the skin, head or ntrails of water a quart Boil to about a pint and a half, remove all from the fire, and when the water is col viper be not a dried one, take away the congealed fa take a chicken of a middle size drawn and the skin wit fat taken off, and put it whole into this decoction wh set it upon the fire till it boils, then remove it from take out the chicken, cut the flesh of it into small piec put again into the water and set it over the fire but as it begins to boil up pour it off, first having tak whatever scum may have risen

VINUM VIPERINUM

Take of dried vipers two ounces, of white wine thr Infuse with a gentle heat for a week, and then wine off

Surbiton, Surrey

A. C. F

## HÆMOLYTIC TRANSFUSION REACTIO

SIR,—I should like to correct the impression, by a statement in Dr Heggie's letter in your Dec 25, that the revised edition of the Medical R Council's memorandum no 9, *The Determin Blood Groups*, has already been published. Th randum is still undergoing revision and the new not likely to be available for some time

Medical Research Council
London, S W 1

JOAN M L
Publications O

## APICAL LOCALISATION OF PULMON TUBERCULOSIS

SIR,—I cannot agree with Dr Cudkowicz's tion (Dec 25) of this phenomenon, with regard has been called "post primary" tuberculosis.

The apical pleural bronchial artery may have a course, but the primary pulmonary tuber does not have a constant position, and may b in any part of the lung Thus there is no the lymph node component of the primary (unless extremely extensive) will be in constant to any small hilar vessel The enlargement and of the bronchial arteries come afterwards, when lesion is of some standing, but are in no way tuberculosis They may occur in any chron disease accompanied by the formation of new tissue—e g, bronchiectasis and pneumoconios

When we come to consider apical "adult tuberculosis generally, we find that doubt h thrown on the view that such a lesion is nec preceded by a childhood infection[1] There is that tissue maturation alone may dictate adult-type apical infection Dr Cudkowicz's will not account for such a case

I feel that the weight of the present evidence the opinion that oxygen lack is the most imp factor

Department of Pathology
Llanelly Hospital

A L W

## ISOBEL CRIPPS CENTRE

Dr Wilfred Barlow writes

It is not surprising that Mr Neil (Dec. 18) members of the medical profession objecting to his of Self Management" Opinions may reasonably diff far doctors can demand a say in matters of mental training for their patients, and a physical or psy "educator" who deals with such conditions as presumably at liberty to disregard the medical pro he chooses But, if he seeks general medical his training as Mr Neil appears to do in his let difficult to see how a case can be made for not the safeguards which are given, for example, by therapists.

I should be the last to deny that the Alexander te of which Mr Neil is one of the many trained teacher be utilised by the medical profession but I would this end achieved by research and by training with safeguards than by advertisement campaigns

The complexity of some of the issues raised here out in the House of Lords report on the Osteop (1935), published by the Stationery Office

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on, T Tough J S *Brit J plast Surg* 1954 7 196
n T Leutner, W *Lancet* 1953 i 700
n t, M B *Lyon med* 1954 192 62

1 Anderson W A D Pathology London

# Obituary

## ARTHUR KEITH

Kt M D Aberd D.Sc LL.D., F R C.S F R.S

IEN Arthur Keith was appointed conservator of the erian museum of the Royal College of Surgeons of nd he was already known to his own profession outstanding anatomist and embryologist. At the ge he won general recognition as an anthropologist Darwinian evolutionist.

was born in 1866 on a small Aberdeenshire farm of the ten children of John Keith 'At the country ols where he began his education he made an pressive showing He was only too willing to upt his lessons to help his father with the harvest when he was 16 he left school to learn to be a farmer the tales of a student who lodged with the Keith y led him to think there might be something in an mic life after all His Latin and the family held, were so poor he could never hope to enter the aculty, but with two years hard he might manage to enter as a nt of medicine His father d him a 'wraith' (term) in leen at Gordon's College to see he could make of it.

1884 after this hesitant start, tered Marischal College where e later wrote John Struthers ned the Darwinian gates for Keith carried off the anatomy prize—the sixth edition of the *of Species*—but he was not one truthers's favourite students ps because he frankly admitted he learned more in the dissecting than in the lecture-room His died at the beginning of his al studies and the major bur hat he won when he topped the rship list eased the family es. In 1888 he took his M.B the highest honours and was led the John Murray medal as ost distinguished graduate of ear

1889 after a few months in general practice he ffered on the recommendation of his professor of y an appointment as medical officer to a mining ny in Siam The flora of the region was imper known and it was essential that the candidate from his medical duties should collect botanical mens for Kew Gardens. At his post at Paron Keith that 80% of the villagers suffered from malaria ransmission by mosquitoes was still unknown o began to dissect monkeys to discover whether were infected His old love of anatomy reasserted and he became a subscriber to the *Journal of my* which he was later to edit He sent some ens to Kew but his real goal was now anatomy e returned to England in 1892 with £150 of savings tinue his studies in the London medical schools.

ides his formal studies at University College in ation for the F.R.C.S he began to read the literature ape world of which his dissections in Siam had him first hand experience Professor Thane gave small room at University College and he obtained es of the primates from the Zoological Gardens to h his data from Siam As an early result of these s he was awarded in 1893 the Struthers medal ze of the University of Aberdeen for his paper ring the ligaments of man and ape The following obtained the F.R.C.S and his M.D degree for his on muscles In 1895 he read Eugene Dubois announcing the discovery in Batavia of a missing Keith came to the conclusion that the fossil skull ntirely human and represented an early stage in evolution From this began his study of the ls of man and his first paper on *Pithecanthropus* was published in *Science Progress* in 1895

The same year the senior demonstratorship in anatomy at the London Hospital Medical College fell vacant and Keith obtained the post. His money was finished and he was desperate to get the job: the entry in his diary ran Got it—thank God; a beginning" Teaching he later confessed did not come easily to him at first but even in those early days he inspired in many of his students, including Frederick Wood Jones, a love of anatomy and research. The following year he was also appointed curator of the college museum and in due course he became joint lecturer and finally head of his department. As a teacher he was anxious to equip his students for clinical practice— I wanted the old practical utility anatomy reintroduced and taught again —and he diverted his research from the evolutionary history of the structures of the human body to their rôle in the living organism In 1901 he undertook a series of X ray investigations to show that the entire diaphragm and not only the right and left domes moved downwards when a breath was taken On this study was based his Hunterian lectures on Glenard's disease (1903) His interest in visceroptosis continued as is shown by the last letter from him which we published (*Lancet* 1953 ii 450). His other work as a practical anatomist included his researches into the mechanism of respiration and into the muscular structure of the heart.

In 1908 Keith left the London Hospital to become conservator of the Hunterian Museum of the Royal College of Surgeons The years at the London had been he held the most critical and profitable of his life but at the College of Surgeons he hoped to be able to turn again to the evolutionary and anthropological problems where his real interests lay He began at once to collect material for an anthropological history and in 1911 he chose as the subject of his Hunterian lectures the Remains of Fossil Man His work at and for the college soon won extramural recognition In 1911 the first and most prized of his six honorary degrees was conferred on him by Aberdeen University, and in 1913 he was elected F.R.S His book on the *Antiquity of Man* was written at this time though it was not published till 1915

The 1914–18 war again shifted the emphasis of his work to practical anatomy War wounds and bone-grafting gave rise to old and unanswered questions and Keith's lectures for these years were published in 1919 with the title of *Menders of the Maimed* In the same years he also published *Engines of the Human Body* But throughout the war Keith continued his anthropological work and as president of the Anthropological Institute (1911–17) he gave four important addresses in which he set out his evolutionary doctrine In 1917 he was appointed to the Fullerian chair of physiology of the Royal Institution which gave him a further opportunity to expound his views. In 1927 as president of the British Association, he reviewed the confirmation offered to Darwin's theories by modern science His growing reputation was shown by the knighthood conferred on him in 1921 The busy round of research writing and lecturing continued till in 1933 owing to ill health he retired from his post at Lincoln's Inn Fields to become master of the Buckston Browne research farm at Downe Here he happily combined work in the study with work in the fields His *New Theory of Evolution* appeared in 1918 and his *Autobiography* in 1950 After the death of his wife in 1931 the interests of the farm furnished him (as he put it) with companionship as well as recreation and the day before he died on Jan 7 he was busy with his pruning hook among the fruit trees

### TRIBUTES

J K writes The value of Sir Arthur Keith's record in the fields of anatomy and anthropology is known throughout the world and wherever the true worth of these sciences is appreciated men honoured and respected him During his long life, packed with such untiring industry and so much rich experience, his contributions inevitably brought him recognition as a worthy successor of Hunter, Darwin, and Huxley, giants of past days, but none of these things could account for that real affection which all who knew him intimately soon discovered they possessed for the man himself

" Like others truly great, neither honours nor achievement changed him. His voice was gentle and soft-spoken, and his transparent humility encouraged those of us who knew so much less than he did to come and slake our thirst for knowledge at the fountain head His lectures in his early days at the Royal College of Surgeons some of us will never forget, and it is their atmosphere, more perhaps than their content, which lingers with us still

" In the old tier-seated theatre, he, if anyone ever did, could make the dry bones live, how he treasured those priceless specimens which he had selected for us with such insight from the museum of which he was the Conservator, and how obviously he enjoyed every moment of the lecture as much as we did! I think ' revelled in ' would be the more apt word to describe the way he spent the all-too-short hour devoted to describing, explaining, and applying the facts of structure and function revealed by each object with its own particular story to illumine a present-day point of clinical application

" Like all good teachers his delivery was natural and completely devoid of tension It gave us the impression of effortlessness No notes were needed, for his princely memory recalled at each succeeding moment what he had already prepared just for that moment as a link in the chain of his exposition or argument, and the impression at the end was that he and we had arrived where we had been told we were going, but that there was still a great deal more our guide could have shown us had time sufficed

" Sir Arthur had that rare gift of being able to make a difficult and complicated subject not only comprehensible but interesting to the uninitiated Those of us who heard his popular lecture at the annual meeting of the British Medical Association in Newcastle in 1921 on the Healing of Prenatal Wounds have never forgotten how with appropriate lantern-slides he made extracts from the story of human embryology not only intelligible but fascinating to the lay members of a very large mixed audience Whether addressing the crowded theatre or in quiet conversation, this great gentleman was always the same happy warrior, characteristically at ease talking about the pursuits he loved and to which he had devoted his life.

" His eyes could on occasion flash fire, for in his contentions for truth his soft-spoken voice could become firm as the grey granite of his native city How firm and yet how kind For this, too, some of us will always gratefully remember him "

R J L writes " During his 25 years as curator of the Hunterian museum, Keith became well known far outside the circle of his scientific contemporaries. His opinions on evolution, and on the nature of man and his place in the cosmos came to be discussed and quoted by many a non-scientific writer He was a staunch Darwinian and an ardent naturalist His reputation spread far and wide, and thousands of pilgrims visited the Museum where he presided like a high priest in his temple He was an accepted authority on human anatomy, but it was as anthropologist and Darwinian evolutionist that he grew to such stature during those years Anthropology and the processes of evolution remained his principal interest until the end of his life

" To visit him in his retirement at the research farm was to find him wearing a battered felt hat, a bird's feather stuck in the hatband, dressed in execrable old clothes, and carrying his four-score years very lightly He was usually engaged in some manual labour about the farm He took a keen interest in the common domestic animals there, having a name for each and studying its character very intently Like most great men he was sympathetic in his understanding and put the most self-conscious person at ease by his natural and ier He was a very kindly man His brain until the end of his life His clean-cut features g gaze marked the incisive brilliance of his o simple commonplace things, and his con- sparkled whether the was highly scientific or concerned the homely things of everyday life general knowledge was profound and his memory pædic His life was active and full until the end remained a trustee of the Hunterian collection continued to write, his last book is now in the

" Few of his contemporaries survive, but a wide of a younger generation, influenced by his charmed by his great personality, will deeply passing "

## CHARLOTTE RHODA BROWN

M D Brux, L R C P E

Dr Charlotte Brown, who died in hospital at on Jan 1 at the age of 86, was one of the early women who qualified in medicine under difficulties despite some opposition

She was a daughter of William Hodgins, of jordan House, co Tipperary, and she never interest in natural history which was bred in her in rural Ireland, in a house with a large garden qualified from the London School of Medicine taking her Brussels doctorate the following year holding several appointments she settled in practice in Bradford, where she was the only doctor, until her marriage in 1901 to the Rev Brown Before the 1914–18 war she did much woman's suffrage movement, and all her life eager to share in any public work in which wome a part

In 1916, she joined the staff of the East Anglian torium at Nayland, and specialised in tuberculosis following year she was appointed tuberculosis officer to the Essex County Council Later she medical superintendent of the children's hosp surgical tuberculosis at High Beech in Epping She remained at High Beech, combining the po a child-welfare appointment, until her retirement practice in 1932 She and her husband then went in Welwyn Garden City, where they took a ver though not a vocal, interest in the activities of neighbourhood

A colleague writes " Dr Brown was a lovable with a large circle of friends in Welwyn. She had a sense of humour, and would tell many stories herself She was excellent company, and her background—the background of the Somerville Ross *Irish R M* stories—gave her an endless anecdote and reminiscence, always very much point, well polished with Irish wit and charm, and kindly and tactful "

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## Appointments

FAIRLAMB A H M B Durh, D P H senior asst M.O., Der
PEDLER C M. H, M B Lond. junior pathologist, In
 Ophthalmology, London
SCHOFIELD P B, M R C.S asst pathologist Inst
 Ophthalmology, London
SEQUEIRA P J L M B Lond S H.M O in pathology, V.D
 ment Royal Free Hospital, London

**Manchester Regional Hospital Board**

FERGUSON, HAROLD, M B Edin, D M.R.D asst
 Blackburn and district hospitals
FREEMAN, GRANVILLE, M A, B M Oxfd, D L.O, F.R.C.S
 time consultant E N T surgeon, Lancaster and
 hospitals
HALL, G J H L, M B Glasg, D.P H D C.H act.
 (Infectious diseases) Ladywell Hospital Salford
 Hospital Wigan
KILPATRICK ALEXANDER L R.C P.E, D A asst
 Lancaster and Kendal hospitals
ROBINSON, FRANK M B Manc F R C.S consultant
 surgeon, south Manchester hospitals
WADDINGTON G H M.R C S, D.M.R.D asst.
 Lancaster and Kendal hospitals
WOODCOCK R C M B Leeds D C P consultant
 Bolton and district hospitals

**Colonial Medical Service**

BANNERMAN, E W Q M.B Edin P.M O Gold Coast
BRANCH P W W M B Lond M O, Barbados
CHARLES R. M F L.R.C.P L., D P H M O, Trinidad
FINLAYSON J D M B M O Sarawak
GRAHAM-CUMMING, GEORGE, M B Edin., D.P.H
 Hong Kong
HARRIS, F C M R C.S, D C P pathologist, ministry
 Gold Coast
HOGG J S, M B Glasg, F R F P.S S.M O Gilbert
 Islands
HUNTER JAMES M B Dubl M O Tanganyika
MURPHY W J D, M B Belf M O Tanganyika
NOBBS N A, M.R C.S asst tuberculosis officer British
SMART, E B, M B F R F.P.S, D P.H specialist Hong
WEBB R. A J, M.B Lond M O, St. Vincent.

# Notes and News

## LASSIFICATION OF PROPRIETARY MEDICINES

HE classification of proprietary preparations which has n undertaken by the Joint Committee on Prescribing is to continued by a standing joint committee of the Health vices Councils. A revised edition of the booklet giving lists reparations classified in categories 1 5 and 6 has been ted and is being distributed to doctors and chemists as uide to prescription under the National Health Service eplaces the lists issued in July 1953 and in January 1954

## REMUNERATION OF HOUSE-OFFICERS

HE Medical Whitley Council (Committee B) have agreed all fully registered house-officers shall be paid at what at present the rate for the third house post—namely 5 per annum They have also agreed that provisionally istered house-officers shall be paid at the rate for the second se post (£475) instead of that for the first house post 5) if they have had suitable experience outside the ional Health Service equivalent to a first house post in service

## FOOT FAULTS

N Dec. 20 Mr W Sayle Creer showed to the general ctice section of Manchester Medical Society a film on *Faults Related to Form and Function* This, he said t with aching and tiredness associated with muscle gue due to over use The film included evidence supporting view that the ligaments of the foot were of paramount ortance the muscles having a subordinate rôle This was traditional English view which went out of fashion when rington showed the importance of reflex muscle action. sed to be said that ballet dancers feet went flat when stood in the relaxed position and their muscles were red Two ballet dancers were shown and it was evident their feet never went flat but merely looked flat owing he ballet shoes The feet of six babies varying in age from lays down to 12 hours showed well formed arches in radistinction to the previously held opinion that at birth es had flat feet, the arch coming into being only by the n of the muscles in the early stages of walking

he lateral stability of the foot depended on the width and rity of the forefoot and it was impaired by narrowness e foot or incompetence of the first metatarsal segment trong foot could be likened to a pair of roller-skates, ng for minimal muscular control a defective foot mbled an ice-skate requiring maximal muscular control op inversion or eversion It was thus overwork and early ue of the muscles that accounted for the symptoms en eye and a critical mind was required in order to assess foot; the standard of normality must be exacting for s *the minor deviations from the normal that had caused* ason When the minor degrees were recognised the cause e symptoms was obvious. Mr Sayle Creer ended with a for greater care of the feet of children because most e were born with healthy feet

## ARTIFICIAL PHOTOSYNTHESIS

Daniel J Arnon professor of plant physiology in University of California announced on Dec 29 at the al meeting of the American Association for the Advance of Science that the process of photosynthesis had been ssfully *duplicated outside* the living plant.[1] He and his iates, after six years research had shown that the ent-containing chloroplasts of green plants could convert on dioxide into sugar even when they were removed the plants cells. Radioactive substances were employed termine the intermediate stages of this process. A new tion— photosynthetic phosphorylation —had been dis red and three catalysts of the reaction had been ified as riboflavine ascorbic acid and vitamin K

## NUFFIELD ORTHOPÆDIC CENTRE

Jan 4 portraits were unveiled of the two men who borated to found the centre Mr A H Smith the chancellor of Oxford University unveiled a portrait of ate G R Girdlestone Sir Robert McCarrison chairman e university s medical postgraduate committee described Girdlestone s orthopædic work was carried out in huts ord Nuffield provided money to rebuild the hospital and s reopened in 1933 as the Wingfield Morris Orthopædic Hospital Prof. J Trueta in unveiling a portrait of Lord Nuffield said that the two men were different in temperament and ideals but between them they had made the hospital what it was today

The portrait of Lord Nuffield by John Whalley has been presented by Lady Nuffield Mr Girdlestone's portrait painted (from a photograph) by Frank Eastman, has been given by old patients and friends

## *CIVILIAN CASUALTIES IN WAR*

THE North West Metropolitan Regional Hospital Board and the Middlesex County Council have lately made a joint study of problems concerning civilian casualties in war The first aid services would operate under the control of the Civil Defence commissioners and controllers and usually medical officers of health would discharge this duty on their behalf Trained nurses and nursing auxiliaries of the National Hospital Service Reserve would be employed in their parent hospitals until called out after an attack The doctors of the mobile first aid units would be general practitioners who would train their teams beforehand The functioning of the casualty transit centres and of the cushion and the base hospitals, with their centres for special cases was described Coördination of plans for managing and treating patients was declared to be essential since life saving and limb saving treatment alone would be practised close to the time and to the place of injury while the continuing treatment for restoration of function would be applied in base hospitals in distant areas all over the country It was conceded that the disposition of hospitals as now planned might have to be altered in the face of a threat of more powerful weapons of attack but it was considered that the principles of employment of first aid ambulance and hospital services would remain unchanged This study was arranged by a directing staff under the chairmanship of Sir Ernest Rock Carling

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### Order of St John of Jerusalem

The Queen has sanctioned the following promotions in and appointments to this Order

*As Knights*—Brigadier R. A Hepple C.B.E. M.C. M.B. W. J Warner, C.B.E. D.S.C.

*As Commanders*—Air Commodore A A G Corbet, M.D Brigadier K. A Hunter O.B.E. M.D R. H Keshen M.D Surgeon Captain E. B Lee M.B. A P Gorham M.B. F M Dearn M.B. R. A I Gray M.B. K G W Saunders O.B.E. F.R.C.S. Lieut Colonel G N Morris F.R.C.S. Lieut Colonel F K Mumford, M.B. R. R. Trail C.B.E. M.C. F.R.C.P

*As Officers*—Lieut -Colonel Stephen Mackenzie O.B.E. M.R.C.S J S Grant, F.R.C.S., Robert Scott Reid M.B.E. M.B. R. A Dench M.C. M.B. Joseph Morris M.B. Lieut.-Colonel J A Melanson M.D Francis O Daly M.B. J A White F.R.C.S J C Moor M.B. Lieut.-Colonel W. R. Everatt, T.D M.B. J C Cassells L.R.C.P.E. Prof Joseph Oakes, M.B.E. M.D, Colonel G A Winfield O.B.E. M.D G D F. Tullis, M.B. V C. J Harris F.R.C.S., A H Penistan M.B. E F Brown M.R.C.P F L Butler M.B. M Y Jaget M.R.C.S., G E. Mullins M.B. Robert Dick M.B., Major M J Bett M.D A L Buchanan, M.B., F.R.C.S R. M B MacLenna F.R.C.P H G Wiltshire M.B. L J Haydon T.D M.B. H E. Offord M.B. J Ripley Oddie M.B. J Trefor Watkins M.B. J H Dixon M.B. R. H. Percival F.R.C.S. J J Kennedy M.B., V C. Meyer M.B. G E. G Peirce F.R.C.S. J McC Caldwell M.B. H F W Robertson M.D

### St George s Hospital Medical School

Postgraduate demonstrations in neurology and psychiatry are being held at the hospital on Thursdays, at 5 P.M during the Lent term. They are open without fees to all doctors and senior medical students

### Chartered Society of 'Queen Square'

The council of this society will shortly hold an election for vacant pensions (£20 per annum) to needy sufferers from incurable nervous diseases. Forms of application may be had from the secretary of the society Queen Square House London W C 1

### Oxford Graduates Medical Club

The winter dinner of this club is to be held on Friday Feb 11 at 7 30 P.M at the Royal College of Surgeons Lincoln s Inn Fields London, W C.2 Prof H R Dean will be in the chair Tickets (25s) may be had from the secretary Mr Selwyn Taylor 3 Roedean Crescent Rochampton S W 15

### Liverpool University Medical Students Society

This society s annual dinner will be held at the Bluecoat Hall Bluecoat Chambers on Thursday Feb 3 at 7.30 P.M The guest of honour will be Mr Arthur Gemmell F.R.C.O.G Tickets (21s) may be had from H Dinnick, Medical School Liverpool University

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[1] New York Times Dec 30 1954

## Fellowships in Clinical Research

The Medical Research Council invite applications for a further series of fellowships in clinical research, tenable at centres in the United Kingdom during the academic year 1955–56 These fellowships are open to suitably qualified medical graduates who desire to prepare themselves for a career in clinical research In general, it is intended that each fellow appointed under the scheme should be given an opportunity, as part of his training for clinical research, to study methods of research in the basic subject most relevant to his particular clinical interest

The awards will be made for one year in the first instance and will be renewable annually in approved cases up to a maximum of three years in all Stipend will be at the rate of £850 per annum, rising by annual increments of £75 to £1000 per annum with superannuation provision in addition

Candidates for these fellowships, which are ordinarily restricted to British subjects resident in the United Kingdom, must be medically qualified and clinically experienced and should preferably have worked for a period in a department in which clinical research was in progress Applicants will be invited to submit their own proposals as to type and place of work, but the Council will be glad to advise successful candidates on the selection of suitable centres of study and to assist in placing them in departments or laboratories where the desired training and experience can be obtained

Applications must be sponsored in each case by the head of the appropriate department in the candidate's university or medical school, and an undertaking will be required that a suitable academic post in a clinical department will be available to the candidate in that institution on satisfactory completion of the period of study under the fellowship

Forms of application may be obtained from the Secretary, Medical Research Council, 38 Old Queen Street, London, S W 1, with whom applications should be lodged not later than March 1

# Diary of the Week

JAN 16 TO 22

### Monday, 17th

POSTGRADUATE MEDICAL SCHOOL OF LONDON Ducane Road, W 12
4 P M Dr Macdonald Critchley Parietal Symptomatology

HUNTERIAN SOCIETY
8 30 P M (Mansion House E C 4 ) Prof Jack Adams Ray (Stockholm) New Symptom Pallor—in the Inflammation syndrome

### Tuesday, 18th

ROYAL COLLEGE OF PHYSICIANS OF LONDON Pall Mall East S W 1
5 P M Prof G M Bull The Uremias (First Goulstonian lecture)

BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P M (London School of Hygiene and Tropical Medicine Keppel Street W C 1 ) Dr Douglas McClean Substances that increase Tissue Permeability and their Relation to Infection and Fertilisation

ST MARY S HOSPITAL MEDICAL SCHOOL Paddington W 2
5 P.M Dr G W B James Neurosis in Gynæcology

INSTITUTE OF DERMATOLOGY St John s Hospital Lisle Street, W C 2
5 30 P M Dr M. S Thomson Tuberculosis Cutis

SOCIETY FOR THE STUDY OF ADDICTION TO ALCOHOL AND OTHER DRUGS
8 P M (11, Chandos Street W 1 ) Dr M M Glatt Treatment Centre for Alcohol Patients at a State Mental Hospital

SOUTH WEST LONDON MEDICAL SOCIETY
8 30 P.M (Bolingbroke Hospital Wandsworth Common S W 11 ) Dr Francis Camps Forensic Medicine and the Law

### Wednesday, 19th

ROYAL SOCIETY OF MEDICINE 1 Wimpole Street W 1
8 15 P.M *General Practice* Dr A Talbot Rogers, Dr F S Cookson Rehabilitation of the Housewife.

INSTITUTE OF DERMATOLOGY
5 30 P M Dr Henry Haber Eosinophilic Granulomas of the Skin

EUGENICS SOCIETY
5 30 P M (Burlington House, Piccadilly W 1 ) Prof L S Penrose F R.S Genetics of Microcythæmia (Thalassæmia)

OXFORD UNIVERSITY
5 P M (Radcliffe Infirmary ) Dr John Bowlby Maternal Care and Mental Health

MIDLAND MEDICAL SOCIETY
8 15 P M (Birmingham Medical Institute 154 Great Charles Street Birmingham 3 ) Sir Stanford Cade Progress in the Treatment of Cancer

ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASGOW, 242 St Vincent Street Glasgow C 2
5 P M Prof W W Mushin Physiological Principles in the Care of the Unconscious Patient (John Burns lecture )

### Thursday, 20th

ROYAL COLLEGE OF PHYSICIANS OF LONDON
5 P.M Professor Bull The Uræmias (Second of two Goulstonian lectures )

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields ondon W C 2
rof Arnold Sorsby Ocular Infections

TGRADUATE MEDICAL FEDERATION
(London School of Hygiene and Tropical Medicine )
D G Melrose Cooling of the Whole Organism

ROYAL ARMY MEDICAL COLLEGE Millbank London S.W.1
5 P M Mr C Naunton Morgan Advances in Surgery in of the Colon and Rectum

BRITISH INSTITUTE OF RADIOLOGY 32 Welbeck Street
8 P M. Dr A H F Marshall Actions of Hormo Pharmacological Agents upon the Acute Skin produced by X Rays and Carcinogenic Hydro Dr L E Houghton Dr J B Walter Mr D E A F INST P Modification of X ray Damage by G Dr Karol Sicher Clinical Trial of A C T H in therapy

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE, House, 26 Portland Place W 1
7 30 P M Prof R M Gordon Mr W Crewe Mr H. Dr B O L Luke, Prof J J C Buckley Sr Manson Bahr Dr Frank Hawking, Dr W E Ke Loiasis

WEST LONDON MEDICO CHIRURGICAL SOCIETY
8 30 P M (Clarendon Restaurant Hammersmith Broadway Dr Dudley Hart Dr C J M Clark (for) Dr Savage Dr J H H Glyn (against) That Mo on Research into Rheumatism has been wasted.

OSLER CLUB
7 45 P M (11 Chandos Street W 1 ) Colonel L W H Neisser and Neisserian Principles in Venereology David Nabarro Decline and Fall of Congenital Sy

UNIVERSITY OF ST ANDREWS, Medical School, Small s Dundee
5 P M Prof R F Tunbridge Problems of Diabetes M

### Friday, 21st

POSTGRADUATE MEDICAL SCHOOL OF LONDON
4 P M Sir Geoffrey Todd Problems of Tuberculous F

ROYAL SOCIETY OF MEDICINE
5 P M *Epidemiology and Preventive Medicine* Dr A Dr A P Goffe Geographical Distribution of Pe litis
8 15 P.M *Radiology* Dr Claude Taylor Dr G D M Dr G W Blomfield Functioning Ovarian other Unusual Growths of the Ovary

FACULTY OF RADIOLOGISTS
5 P M (Royal College of Surgeons of England ) *Radio* Mr George Seed Dr J R Nuttall Cancer of the

INSTITUTE OF DERMATOLOGY
5 30 P M Dr G B Mitchell Heggs Chronic Granu

ROYAL MEDICAL SOCIETY 7 Melbourne Place Edinburgh
8 P.M Prof D M Dunlop Cortisone in Practical

ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASG
5 P M Mr W S Mack Surgery of the Bladder and Pro

### Saturday, 22nd

BRITISH ASSOCIATION OF ALLERGISTS
11 A.M (1 Wimpole Street, W 1 ) Papers.

## Anglo-French Exchange Bursaries

Short-term grants for work in France are offered year to British doctors and medical research workers Institut National d'Hygiène, Paris Details can be had Dr G W Wolstenholme, Ciba Foundation, 41, Port London, W 1 The closing date for applications is Feb

## Mental-health Campaign in Edinburgh

In February a campaign is to be staged in Edin with the aims of educating the public about the mental illness and of recruiting nurses for mental ho This campaign is being organised with the help of re tatives of the hospitals concerned, the churches, bodies, the South Eastern Regional Hospital Boa Ministry of Labour, the Department of Health for Sc the Scottish Information Office, the General Board of C and the Scottish Association for Mental Health

Mr B W Rycroft has been invited to become an member of the Ophthalmological Society of South Africa

The Association of Universities of the British Comm (36 Gordon Square London, W C 1) have published a list of for advanced study and research including fellowships sch and grants The list will appear as appendices II and III *Commonwealth Universities Yearbook*, 1955

*A reference list of publications and organisations* conc cell and tissue preservation has been compiled by the Producers Association (295 Madison Avenue New York, U S A ) from which copies may be had

CORRIGENDUM *Diagnosis of Pericardial Effusion*—I annotation of Jan 8 the last paragraph should have 'Although pericardial effusion causing tamponade is uncom

# Births, Marriages, and Deaths

## BIRTHS

WARREN BROWNE.—On Jan 8 at King s College Hospital, to James M B Edin wife of Dr D Warren Browne I O W —a daughter

## DEATHS

WHITE —On Jan 6 at Sutton Surrey, Robert George M.A , M B B.SC in his 80th year

# RRELATION OF RADIOLOGICAL AND ATHOLOGICAL CHANGES IN SOME DISEASES OF THE LUNG*

J Gough
M.D Wales
SOR OF PATHOLOGY WELSH NATIONAL SCHOOL OF MEDICINE CARDIFF

several years I have been using paper mounted s of lungs with the particular aim of comparing orbid anatomical changes with the radiological es found during life

technique of cutting sections of whole organs is old. It was used by Richard Muir in 1884 His s were mounted on glass and specimens of the que still exist in the pathology department at urgh University There are similar ones in the ment of pathology at Cambridge where they were by Professor Sims Woodhead The method was ntly not extensively employed and even when d and modified by Christeller in 1924 it did not o widely popular The preparations were first used e demonstration of changes seen by naked eye out 1924 the method was modified by T C Dodds preparation of large sections thin enough to be e for microscopy This is the method adopted ance by Cheatle and Cutler (1931) for investigation inoma of the breast

method now used (Gough and Wentworth 1948) o original features the sections are mounted on and not on glass and certain glycol derivatives ed to preserve the natural colours Staining is unnecessary, although stains can be used for special es such as the demonstration of hæmosiderin prussian blue technique These paper mounted s are now being produced in many centres in and abroad and their popularity is probably part to the simplification of the technique but to the ease and convenience of handling and paper preparations as compared with glass The s can be stored like other paper and those which kept in book form have not deteriorated during ht years since the technique was started The s can be conveniently filed with the corresponding aphs Since many sections can be obtained from k of tissue they form a convenient medium of ge between centres working on similar problems

primary object was to collect a large number of s of lungs from coalminers in order to interpret diological appearances of pneumoconiosis but I ere speak principally of other conditions which een investigated in the same way

## Mitral Stenosis

iderable interest is shown at the present time in lmonary changes associated with mitral stenosis, these lung changes undoubtedly contribute to spnœa The punctate picture due to hæmosiderin lungs is a familiar one and large sections show the distribution of the pigment which produces iological shadows More dense opacities and rather ones may be seen particularly in the lower lung Some have described the two types of shadow enting different degrees of hæmosiderosis (e.g nd Levine 1950), but anatomically it is seen that se shadows correspond with areas of ossification use of these is not known but their recognition ographs is of some importance because they may lso be mistaken for foci of tuberculosis

In some cases of mitral stenosis the lung fields show linear markings particularly in the lower parts where a series of parallel lines run in from the chest wall above the costophrenic angles Sometimes these are very sharply outlined and about a millimetre in thickness When I have asked some of my radiological colleagues what they represent, they say they are Fleischner's lines and that they represent areas of plate-like atelectasis It is true that Fleischner described such areas of atelectasis but these produce much wider and often longer areas of radio-opacity and no one more than Fleischner (1954) was puzzled by these thin lines in mitral stenosis which he was sure were not due to atelectasis although for many years he could not find an anatomical explanation It was from a study of paper mounted sections that he obtained the solution When examining some of the preparations of coalminers lungs which had been prepared in my department he was attracted by the deposition of coal in the septa between the secondary lobules, and he noted that in some cases of mitral stenosis hæmosiderin had a similar distribution and that this deposition corresponded with the position of the lines in the radiographs The large sections of lungs of coal miners are indeed very helpful in delineating some of the anatomical features in the lung In the majority of coalminers the bulk of the dust collects towards the centres of the secondary lobules especially in relation to the terminal and respiratory bronchioles (Heppleston 1953) but some of the dust accumulates in the lung septa, and in a small proportion of miners this is the main site of deposition. Likewise with hæmosiderin in most lungs it is in the form of foci in the centres of the lobules but in some it is mainly in the septa

Fleischner believed that not all the lines in mitral stenosis radiographs were due to hæmosiderin he thought that some might be due to œdema of the interlobular septa but he did not have material to show this I have however, obtained sections corresponding with radiographs taken during life to show this appearance which consists in œdema of the connective tissue of the septa together with marked distension of the lymphatics This type of line is often transient in radiographs being present during periods of cardiac failure but disappearing when there is recovery from the œdema It will be interesting to see whether the persistent lines due to hæmosiderin disappear after successful valvotomy

## Microlithiasis Alveolaris Pulmonum

The need for careful correlation of radiological and pathological findings is illustrated by the following example

In Shanks and Kerley's *Textbook of X ray Diagnosis* (1951) is a radiograph said to be of gross chronic hæmosiderosis of the lungs in a woman of 56 with mitral stenosis The lungs were intensely radio-opaque The diagnosis was based on biopsy material obtained by needle puncture. This woman has since died and an account of the post mortem findings is given by Sharp and Danino (1953) The lungs were of very unusual appearance The cause of the radio-opacity was the development of calcispherites and bone in the lung a rare condition which has been described previously in German literature under the title—microlithiasis alveolaris pulmonum (Lelcher 1949) The amount of hæmosiderin in the lungs of Sharp and Danino's case was small When sections of the lungs were mounted on paper they felt exactly like sandpaper ; the material however had not been inhaled but was endogenous and composed of calcium phosphate and calcium-carbonate The association with mitral stenosis may well have been fortuitous for other cases described have not had associated heart-disease

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er read before the Midland Tuberculosis Society on 6 1954

In several radiological centres in this country and in the United States this condition had not apparently been encountered, but I had an interesting experience in one U S centre when I showed the radiograph at a seminar Although none of those present knew of microlithiasis alveolaris pulmonum, one of them was able to go to the archives of the department and produce a similar picture which for many years had lain there labelled " ? severe ossification in tuberculosis "

The memory of particular pictures is, of course, as great an asset to the radiologist as to the morbid histologist, and one wonders when a radiologist is puzzling over an unusual film whether he tends to think mainly of similar pictures he has seen before or whether he tends to think in terms of the underlying pathological change Paper-mounted sections filed with the corresponding radiographs may provide a useful reminder of the morbid anatomy In order to make headway in the correct interpretation of radiographs it is necessary to collect and store them so that they will be available when the pathological evidence is eventually obtained Hospital committees discuss how long radiographs should be kept, and I am disturbed at suggestions of a limit of this or that number of years In the study of a chronic disease like pneumoconiosis radiographs taken very many years ago are now proving of great value

### Emphysema

In the study of coalminers' lungs I have been interested not only in the deposition of dust but also in the emphysema that results It has been shown (Gough, James, and Wentworth 1949) that the simple postero-anterior radiograph is not a reliable means of assessing the degree of focal emphysema which occurs in coal workers, and indeed that type of radiograph appears to be unreliable in the diagnosis of emphysema of all sorts Knott and Christie (1951) have shown the inaccuracy of postero anterior radiographs in the diagnosis of emphysema

Such diagnosis can be made more accurate with radiographs taken in inspiration and expiration and both postero-anterior and lateral, but even if accuracy in deciding the presence of emphysema were obtainable in this way that is only part of the answer What sort of emphysema is it ? I have compared the lungs of people dying from the emphysema associated with chronic bronchitis with those dying in status asthmaticus I understand that radiologically chronic bronchitis and asthma do not show two distinct types of radiotranslucency, but anatomically the changes in the two are quite different Of a consecutive series of 17 cases of fatal status asthmaticus, bullous emphysema was present in only 1, and in this case there was associated severe bronchiectasis In the other cases the lungs were simply over distended just like those of a person drowned Indeed, it seems to be the most commonly accepted view that death in status asthmaticus is a form of drowning due to the tenacious mucus which the asthmatic cannot expel There was, however, no breakdown of the lung tissue to form bullæ, which is in striking contrast to the emphysema of chronic bronchitis The importance of this seems to be that the inflation of the lung in asthma is a reversible condition, whereas the destructive processes in the lung of chronic bronchitis seems to be permanent Lodge (1946) has shown that the appearance of the blood-vessels in radiographs in emphysema is different from that in asthma, but otherwise the appearance in lung fields is similar in the two conditions With chronic bronchitis and emphysema as one of the more important causes of death and morbidity, it is important that more should be learnt about it and there is need ological technique to help in distinguishing various of emphysema and to show at what stage processes take place

### Uræmic Œdema

Œdema of the lungs produces various app radiographs, and one of the more interesting central œdema which occurs in uræmia, " butterfly " appearance The histological descr the condition has been given by Doniach Recently, Herrnheiser and Hinson (1954) have gated the gross anatomy of this condition, mounted large sections They were able to show the distribution of the œdema They descri anatomical distribution of the lesion and relat the conception of the lung anatomy according each lobe is divisible into a lobar root, a cortex They found that the œdema in this limited to the medullary part These investigat those of Prichard, Daniel, and Andran (1954) the possibility of explanation of some of the findings which emerge when the circulation in is disturbed in man and in laboratory animals.

### Tuberculosis

I have not used the technique for any investigation into tuberculosis apart from coal but have prepared large sections for some centre the excision of lung is carried out The metho suitable for small segments, because expansion lung is required to obtain satisfactory results. lobe or a whole lung is removed, however, the tions have been quite satisfactory They can with the radiographs and may be of value results of a large series of cases are being Where very detailed study is required, serial several blocks of tissue may be used In this can be shown at least how much diseased and healthy tissue has been removed The section very effectively whether bronchiectasis is a the tuberculosis, and so may help in deciding cases do well and others not so well

When I first demonstrated the paper-mounted about eight years ago, doubt was expressed could do much for research, because they outmoded field of morbid anatomy I hope the given show that the researches have been measure profitable, and that the very large lung sections that we have built up has served, continue to serve, as valuable material both in path and radiological studies

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" . too often the youth organisations failed to recognize the great weight that 'modernity' ca average artisan home, symbolizing as it does that that the working class family of the past was on achieve by great self sacrifice or by a fluke 'Mod so vital a word to these boys and girls, and to m adults of their world, that it behoves any unit which to teach the good life to appear up to-date itself as the youth organisations' activities did not sound fa ones, in so far as its set-up was authoritarian and tion old fashioned, and in so far as its physical se slovenly, the unit lost respect "—PEARL JEPHCO *Young People* London, 1954 , p 128

# TMENT OF ACUTELY PERFORATED PEPTIC ULCERS

## DIOLOGICAL DIAGNOSIS OF SITE OF PERFORATION

H D MOORE
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*With illustrations on plate*

purpose of this paper is to recount the experience and conclusions of one surgeon in the treatment erent methods of perforated peptic ulcers and to e a radiological technique to diagnose the site o tion.

series consists of 125 patients of whom 65 were by aspiration, 45 by simple suture of the perfora nd 15 by immediate partial gastrectomy Those by aspiration and those treated by simple suture nselected aspiration was used for all patients d to the beds of Prof P J Moir in the last three and simple suture for all patients in the beds of urgeons who regarded it as the method of choice mmediate partial gastrectomies however were a y selected group admitted to the service of Prof Chamberlain.

### Conservative Non operative or Aspiration Treatment

good accounts of the management and progress ents treated in this way have been given (e g Taylor 1940), but a few points need to be ted

dose of morphine must be large (gr $^1/_4$ for men or women intravenously) to produce comfort and spirations Only one dose is given unless the in charge of the case expressly orders otherwise on is done with a no 11 œsophageal tube and by ple three-bottle method (fig 1) A large tube is ry because the stomach contents are often glairy ink and the suction must be continuous so as to the fluid and *gas* as they collect—especially the ich these patients swallow This seems to be nt for Hermon Taylor (1951) had 2 patients, and et al. (1952) 1 who continued to leak air into itoneum and died (these workers used intermittent only) It is of course important to make sure e tube is in the dependent part of the stomach, y changing its position until it is working well using a radio-opaque tube and X ray control 5)

ys are used as a diagnostic control (the special gical diagnosis of the site of perforation is dis below) 63% of cases showed free intraperitoneal metimes a considerable amount (fig 2) without the progress in any way It has not been neces- take frequent radiographs as was done by Taylor (1951), progress is judged clinically

RESULTS

atients were treated conservatively The diag criteria are shown in table I and the results in . No case has been included where there was any about the diagnosis. The average time in hospital teen days 58 patients made an uninterrupted y; 2 were started on the conservative method re sutured some hours later; 2 had a subphrenic ; and 3 died (4 6%)

tients with early perforations had their treatment d (at nine hours and at twenty four hours) because ing pain and rigidity suggested that the ulcers ot sealed despite the patients excellent general on but at operation the perforations were found losed There was a small local collection of fluid, gas and fibrin in the region of the hole and above the right lobe of the liver but the intestines were clean and shining and there was no apparent cause for the persistent pain and rigidity The time on conservative measures did not affect their progress in any way

2 patients developed a subphrenic abscess The first, with a fifteen hour perforation formed an abscess directly which was drained he was in hospital two months The second had an eleven hour history, did very well on conservative treatment and was discharged in seventeen days It was known that he had persistent subphrenic gas and fluid but previous experience had shown that these are usually absorbed In his case, however this did not happen and he was readmitted twelve days later when the abscess was drained He was in hospital for a total of two months

Subphrenic gas often with a fluid level was present in 63% of patients It is almost always absorbed without incident even when present in large quantities (fig 2) As serial radiographs were taken in only a few cases

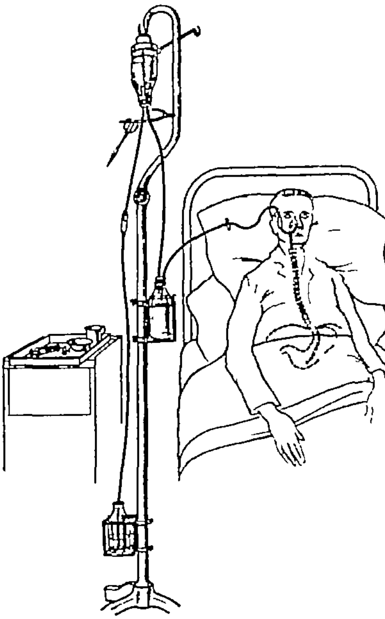

Fig 1—Three-bottle continuous-suction apparatus.

The bottles are the ordinary litre saline bottles. It is important to have the long down tube under water in the lower bottle; otherwise the water runs out. When the top bottle is empty it is simply changed with the bottom one; but it is necessary to clip the in and out tubes near the [illegible] bottle when changing; otherwise the negative pressure [illegible] the system is lost and half a bottle of water runs out [illegible] it leading to frequent changing (hence the Spen[illegible] forceps hanging on the drip stand). All glass [illegible] between the patient and the first bottle must [illegible] rest do not matter

A sterile syringe adaptor, and saline [illegible] syringe through the stomach-tube if it [illegible] and the nurses must realise that it [illegible] test drink is given and then a few [illegible] aspiration of water as well as fluid [illegible] hindered by running down the [illegible] [illegible] it is not possible to say how long the gas usually remains, but it was present, with a fluid level in 6 cases for 8, 8, 12, 14, 20, and 29 days These patients were well, with normal temperatures and leucocyte counts, and cleared without interference, but this should not lead to over confidence, as the second subphrenic abscess showed, and it would be wise to screen all perforations before discharge, to exclude an unrecognised or unresolving subphrenic collection

3 patients died (4 6%) They were men aged 43, 73, and 33, with perforations of five, six, and fifteen hours respectively, and they were alike in all being ill on admission from the peritoneal effects of the perforation—2 with a low blood pressure and rapid pulse but a short history, and 1 with a long history and beginning distension of the abdomen A 4th patient should be considered here, who is included in the results of simple suture This was a woman, aged 69, whose ulcer had p only one and a half hours previously but who was too ill for operation, because of peripheral She was treated conservatively *only* because she w She died in twenty four hours

TABLE I—DIAGNOSTIC CRITERIA FOR NON OPERATIVE TREATMENT OF PERFORATED PEPTIC ULCERS PATIENTS WITH TYPICAL HISTORY AND PHYSICAL SIGNS

| Free gas under diaphragm | | No free gas but pain referred to shoulder | | No free gas or shoulder pain but subsequent radiol confirmation of ulcer | No gas or shoulder pain and no later radiol proof |
|---|---|---|---|---|---|
| 41 | 27 barium meal positive<br>7 barium meal negative<br>7 barium meal not done | 6 | 4 barium meal positive<br>2 barium meal negative | 13 | 5 |

TABLE III—MORTALITY OF NON OPERATIVE PATIENTS THOUGHT TO BE TOO ILL FOR OPERAT PERITONEAL EFFECTS OF PERFORATION

| Reference | Usual treatment of choice | No. thought unfit for operati |
|---|---|---|
| Gill and Jenkins (1950) | Conservative | 3 |
| Taylor (1951) | ,, | 4 |
| Stead (1951) | ,, | 6 |
| Seeley (1951) | ,, | 4 |
| Heslop, Bullough, Brun (1952) | ,, | 5 |
| Nuboer (1951) | Gastrectomy | 3 |
| Graham (1946) | Suture | 2 |
| Baritell (1947) | ,, | 1 |
| Avery Jones et al. (1950) | ,, | 13 |
| Vaughan and Warren (1951) | ,, | 9 |
| Armitage (1954) | ,, | 13 |
| Total | | 56 |

THE BAD RISK

These 4 cases suggest that patients who are ill from the effects of the perforation—i e, with circulatory failure or with an infective ge peritonitis—will die if treated conservatively, is supported by the fact that in 56 published perforation (table III) in which the patient was to be too ill for operation, there were only 2

It seemed to me, therefore, that such patients be operated on and not treated by aspiration, following 3 cases were so treated with gratifying

TABLE II—RESULTS OF DIFFERENT TREATMENTS IN 125 PERFORATED PEPTIC ULCERS

| Year | No of cases | Age (yr) | Sex | | Time since perforation (hr) | Site of perforation (at operation or from barium meal when done) | | | Results | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | M | F | | D U | G U | Jej | Uninterrupted recovery | Complications | Died | Details of deaths |
| *Non-operative treatment* | | | | | | | | | | | | |
| 1951 | 17 | 26–69 (av 44) | 16 | 1 | 1–15 (av 3½) | 8 | 1 | | 15 | | 2 | Male aged 43 D U 5 hr perf Male aged 73 G U 6-hr perf Both ill |
| 1952 | 24 | 23–73 (av 44) | 19 | 5 | ½–26 (av 5) | 12 | 2 | 1 | 21 | One case Oper after 9 hr on aspiration One subphrenic abscess in man, aged 52, with 15 hr perf. | 1 | Male 33 D U 15-hr perf Ill |
| 1953–54 | 24 | 25–66 (av 42) | 23 | 1 | 1½–48 (av 7) | 14 | 1 | | 22 | One subphrenic abscess in man, aged 58, with 11 hr perf. One case operated after 24 hr on aspiration | 0 | |
| Total | 65 | Av 43 | 58 | 7 | Av 5 | 34 | 4 | 1 | 58 | 4 | 3 | |
| *Simple suture* | | | | | | | | | | | | |
| 1950 | 7 | 25–60 (av 41) | 5 | 2 | Not stated | 6 | 0 | 1 | 6 | | 1 | Female aged 69 1½ hr perf. D U v ill not operated on |
| 1951 | 19 | 27–65 (av 47) | 17 | 2 | 2–20 (av 5) | 16 | 2 | 1 | 17 | Burst wound in man, aged 53, with 7 hr perf D U | 1 | Male, aged 63, with 20 hr perf D U, died 8th day |
| 1952 | 10 | 26–66 (av 42) | 6 | 4 | 1–12 (av 4) | 10 | | | 10 | | 0 | |
| 1953–54 | 9 | 33–75 (av 51) | 5 | 4 | 2–48 (av 14) | 6 | 3 | | 7 | One case of subphrenic abscess in female with 18 hr perf D U One case of pelvic abscess in man, aged 44, with 48 hr perf. D U | 0 | |
| Total | 45 | Av 46 | 33 | 12 | Av 8 | 38 | 5 | 2 | 40 | 3 | 2 | |
| *iate partial gastrectomy* | | | | | | | | | | | | |
| 4 | 15 | 24–70 (av 45) | 14 | 1 | ¾–7 (av 3) | 14 | 1 | | 14 | Postoperative pneumonia in 1 case | 0 | |

e 1.—A man, aged 44 was sent to hospital with a sis of acute retention of urine because he had passed ne for twenty four hours, and had abdominal pain and apubic swelling dull to percussion. He had in point a peptic ulcer which had perforated forty-eight hours The lack of urine was due to anuria and the supra swelling which was present only when he sat up was ritoneal fluid he was gravely ill, with unrecordable pressure He was given morphine gr 1/4 put on uous gastric suction and antibiotics and given three pints of blood and two pints of dextran which brought his blood pressure to 100/70 mm. Hg Laparotomy was done three hours after admission the fluid was sucked out of the peritoneum, and the perforation was sutured He recovered and his postoperative course was not unduly difficult

Case 2 —A woman, aged 51 with an eighteen hour perforation was gravely ill with pulse rate 124 blood pressure 85/65 and a somewhat distended abdomen. She was given morphine and antibiotics, and put on continuous gastric

TABLE IV—MORTALITY AND MORBIDITY IN 2750 PERFORATED PEPTIC ULCERS

| Reference | Years concerned | No of cases | No of deaths | Details of deaths |  | Morbidity |  |
|---|---|---|---|---|---|---|---|
|  |  |  |  | Where recovery was expected | Where death was expected | Severe | Probably less severe |
| *erative treatment :* |  |  |  |  |  |  |  |
| 1 Turner (1945) |  | 6 | 0 |  |  | Nil |  |
| (1946) |  | 14 | 2 = 14% | D U 7 hr perf. operated after 5 hr pneumonia<br>G U continued leak |  | 1 abscess (intraperitoneal) |  |
| Jenkins (1950) |  | 21 | 5 = 20% |  | 3 late perfs., very ill<br>2 perfs. plus severe bleeding | Not given |  |
| (1951) |  | 72 | 7 = 10% | 2 air swallowers<br>1 pneumonia | 3 late perfs. very ill.<br>1 severe shock | 3 abscesses |  |
| 1951) |  | 50 | 5 = 10% | 1 failed treatment | 4 too ill for operation (3 G U 1 D U) | 3 abscesses |  |
| (1951) |  | 110 | 5 = 4 5% | 1 failed treatment | 4 moribund on admission | 6 abscesses<br>4 pleural effusions<br>1 pneumonia<br>1 phlebitis |  |
| et al (1952) |  | 124 | 9 = 7% | 1 air swallower<br>3 abscesses drained giving pancreatic fistulæ | 5 late perfs. very ill (3 G U 2 D U) | 3 abscesses |  |
| series |  | 65 | 3 = 5% | 1 D U —5-hr perf. | 2 very ill on admission | 2 abscesses |  |
| tal |  | 460 | 30 = 7 7 % | 12 failure of method in 460 cases = 2 6 % |  | 20 of 442 cases = 5 9 % |  |
| *suture* |  |  |  |  |  |  |  |
| (1947) | 1944–47 | 88 | 2 = 2 3 % |  | 1 mitral stenosis and pulmonary œdema<br>1 man 63 Not operated. 2 or 3 days perf | 1 burst wound<br>4 abscesses<br>4 pneumonias | 9 wound infections<br>3 lobar collapse of lung |
| Jones et al. (1950) | 1947–48 | 116 | 11 = 10% | 2 from wound infection and chest troubles | 2 from severe bleeding<br>7 not operated on too ill from perf or medical state | Nil | 42 chest troubles<br>8 wound infections |
| and Warren (1951) | 1944–49 | 81 | 3 = 3 7% | 1 peritonitis | 2 too ill for operation | Not given |  |
| nd Payson (1952) | 1941–46 | 70 | 5 = 7 1% | Not given | Not given | 7 pneumonitis<br>2 abscesses<br>7 wound dehiscence<br>1 duod fistula | 11 wound infections |
|  | 1940–50 | 97 | 7 = 7 2% | Not given | Not given | 6 pneumonitis<br>3 abscesses<br>1 burst wound<br>1 duod fistula | 9 wound infections |
| (1952) | 1947–51 | 60 | 4 = 6 7% | Not given | Not given | Not given |  |
| et al. (1952) |  | 104 | 9 = 8·6% | 3 short history died of peritonitis<br>2 short history—well—sudden postop death. 1 long, reperf on 13th day | 1 man 50 auric fibrillation. 1 man 61 G U 5 hr perf. shocked. 1 man 27 D U 27 hr | 1 burst wound<br>2 abscesses<br>1 incisional hernia | 1 infected wound<br>9 paralytic ileus |
| t al (1953) | 1942–51 | 88 | 17 = 17 5% | 3 pulm emboli<br>1 intest. obstr<br>1 hydropneumothorax | 3 severe bleeding<br>4 heart-failure<br>4 peritonitis (pre antibiotic)<br>1 carc œsoph with lung collapse | 1 duod fistula<br>5 phlebitis<br>3 pulm emboli<br>3 pneumonitis<br>2 abscesses | 13 wound infections |
| et al (1953) | 1941–45 | 114 | 2 = 1 8% | 1 perf. 5 hr | 1 perf 30 hr Male 65 | Not given | Not given |
| (1953) | 1946–50 | 206 | 13 = 6 3% | None in young early acute ulcers Mort rose with age length of perf., and history of ulceration |  | Not given | Not given |
| series | 1950–54 | 45 | 2 = 4 4% | None | 1 female 69 perf D U 17 hr Shocked—not operated on<br>1 male 63 D U 20 hr | 2 abscesses<br>1 burst abdomen | Nil |
| Total |  | 1068 | 75 = 7% | 15 of 633 cases = 2 4% Where method failed |  | 5 0 of 607 cases = 9 7% | 105 of 607 cases = 17 3 |
| *ate partial gastrectomy* |  |  |  |  |  |  |  |
| (1939) | 1933–36 | 937 | 84 = 8 9% | Not given | Not given | Selected cases. Morbidity not given |  |
| and Thompson (1936) | 1936 | 17 | 1 = 5·8% | Not given | Not given | Jejunal ulcers. Morbidity not given |  |
| (1941) | 1941–42 | 12 | 2 = 17% | 1 male 45 Perf 7 hr<br>1 male 38 Perf 5 hr | Nil | Selected cases Morbidity not given |  |
| (1951) | 1940–47 | 69 | 4 = 5 7% | Not given | Not given |  |  |
|  | 1947 51 | 65 | 4 = 6 | 1 case Details not given | 3 moribund on admission No operation | Unselected Morbidity not given |  |
| (1952) | 1952 | 41 | 0 | Nil | Nil | Selected. Morbidity not given |  |
| anopoulos and topoulos (1952) | 1952 | 69 | 2 = [illegible] 9% | 1 case where details not given. 1 male 7[illegible] [illegible] | Nil | Selected Morbidity not given |  |
| series | 1950–51 | 15 | 0 | Nil | Nil | Selected. | 1 postoperative pneumonia |
| Total |  | 1[illegible]25 | 97 = 7 9 | 5 of [illegible]02 cases = 2 5 Where method failed |  |  |  |

suction Two pints of blood were given, and the systolic blood-pressure rose to just above 100 mm Hg in about an hour Laparotomy was done, the peritoneum sucked clear, and the perforation sutured She was given two more pints of blood and two pints of dextran, and her blood-pressure, which had fallen with the anæsthesia, rose to 110 mm Hg and was maintained thereat She was discharged well a month after admission.

Case 3 —A woman, aged 36, was admitted on March 24, 1954, with three days' severe abdominal pain. She was gravely ill, with cold extremities, respirations 28 per minute, pulse rate 130–140, and systolic blood pressure below 100 mm Hg Her abdomen was tender all over, distended, and silent; a diagnosis was made of generalised peritonitis with paralytic ileus, probably arising from a perforated peptic ulcer She was given morphine and antibiotics and put on continuous gastric suction and intravenous dextran, and laparotomy was begun without waiting for the blood pressure to rise She was found to have generalised peritonitis with much free bloodstained peritoneal fluid, arising from strangulation of a loop of jejunum. This was resected, and, after a further three pints of dextran, two pints of blood, and a litre of saline solution given rapidly, her condition improved and remained satisfactory The postoperative course was singularly smooth, and she was discharged a month later

This last case is included here partly because of the mistaken diagnosis but mainly because the woman was, by the usual criteria, much too ill for operation

### COMMENT

The above results of the conservative treatment indicate that

(1) The usual course is easy and without anxiety

(2) Subphrenic gas and fluid are common (63%), but only in an occasional case are they not absorbed spontaneously Nevertheless these collections must be watched with care

(3) The patients who die are the ones who are ill on admission from the effects of the perforation These are the cases generally and widely treated by aspiration (the "forced conservative" method) and are the very ones who should *not* be treated by this method

## Simple Suture

The preoperative and postoperative treatment of these patients is the same as that of those treated by aspiration, except that less morphine is given The perforation was closed by simple transverse infolding, reinforced with an omental plug, and the peritoneal cavity was cleared of all free fluid I would add that I have never seen the peritoneum full of beer and carrots, which the opponents of the non-operative method so picturesquely describe Indeed, I have seldom been able to recognise stomach contents in the peritoneum

### RESULTS

As table II shows, 45 patients were operated on, and the average time in hospital was fifteen and a half days 40 had an uninterrupted recovery, 1 patient burst his wound, 2 developed abscesses, and 2 died (4 4%)

The "burst abdomen" was in a man, aged 53, with a seven-hour perforation There seemed to be no cause for this, and he recovered after resuture

The 2 cases of abscesses are those I have already cited to show that peritoneal toilet and suture of the perforation offer the only chance of survival where the patient is gravely ill from the peritoneal effects of the perforation Their perforations were of eighteen and forty-eight hours' standing, and both were desperately ill with gross peritonitis Their abscesses resolved without operation, but they were in hospital for forty and thirty days.

The 2 patients who died were a man aged 63, with a perforation for twenty hours, and a woman aged 69, with perforation for an hour and a half, both had long ulcer histories The man died in eight days from peritonitis The woman was treated conservatively *only* because she ught to be too ill for operation, and died within ur hours (see above)

### COMMENT

These results of simple suture of perforations that

(1) The usual course is easy and without anx

(2) From time to time complications arise which to be unavoidable, either because the cause is (e g, the burst abdomen) or because the patient late (e g, abscesses in late perforations)

(3) Some deaths seem at present to be (e g, the 8th day death from peritonitis in a stood his operation well and whose perforation sealed but who could not cope with the in the use of antibiotics), and some deaths avoided by bold measures (e g, operation in desperately ill from the peritoneal effects of the

## Partial Gastrectomy

Only patients who had perforated within and were in good condition were submitted to tomy Hence this group is highly selected

Although patients with perforated ulcers stated to be "shocked," they have, apart neglected perforation (and the occasional early normal blood-pressure and relatively slow agrees with the findings of Estes and Bennett

For gastrectomy the preoperative and post care is the same as for the patients treated by but with two differences (1) the preoperative is less, and (2) gastric suction is not used unless the patient vomits

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## LEGENDS TO ILLUSTRATIONS ON P

### MR MOORE

**Fig 2—Perforated duodenal ulcer**

The patient is erect and has been given viscous 30 ml and water 30 ml, showing very large amount intraperitoneal gas and retention of diodone in This patient was treated by aspiration and well in 14 days

**Fig 3—Duodenal perforation**

Left radiograph, with patient erect, shows st duodenal cap outlined and a little gas just above radiograph, with patient supine, suggests leak of peritoneum (confirmed at operation)

**Fig 4—Prepyloric perforation**

Erect (left) and supine (right) films with 30 ml and water 30 ml. Diodone has not passed denum, and there is spasm of middle of stomach (at there was no abnormality at this site) Tube is into fundus Erect film shows no escape of supine film, taken 7 minutes later, shows escape of headwards and to left of vertebræ from prepyloric ulcer

**Fig 5—Perforated gastric ulcer**

Ulcer is well outlined on lesser curvature just beyond tip of stomach tube Diodone fills pyloric region mediate part of stomach is empty Diodone has peritoneum and is lying near lower part of left iliac fossa The stomach tube should go down.

**Fig 6—Normal**

Outpatient attending for barium meal, which normal Viscous diodone 30 ml and water 30 ml given, outlining stomach, duodenal cap, and duo

**Fig 7—Duodenal perforation**

No tube has been passed Patient has diodone and is supine Stomach contains a go fluid, and diodone is escaping through duodenal and passing headwards towards a collection of air vertebræ

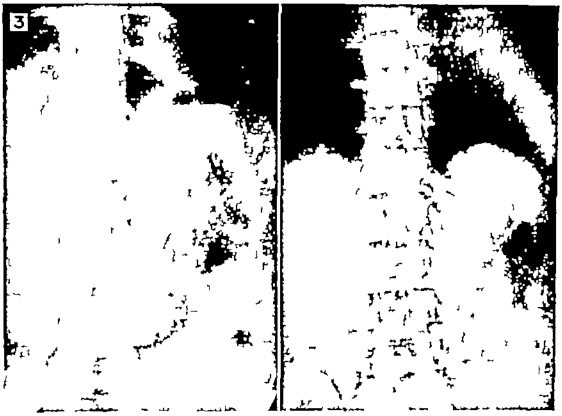
**Fig 8—Perforated duodenal ulcer**

Diodone in stomach and small bowel and duodenum, capped by air bubble and spreading 12th rib Note gas under diaphragm, and left renal

MR MOORE

UTE PERFORATED
PEPTIC ULCERS

3



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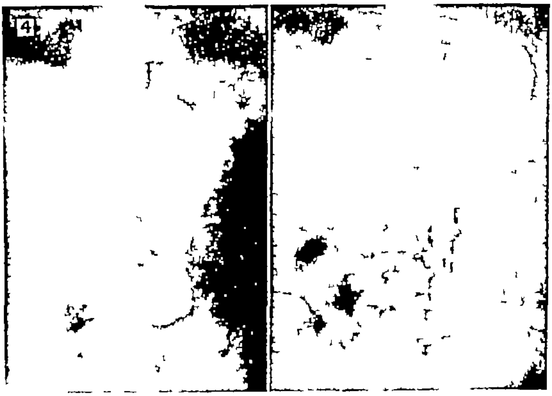

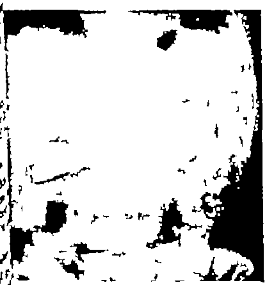

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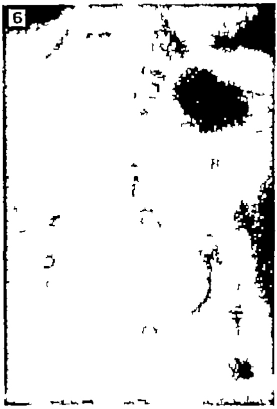

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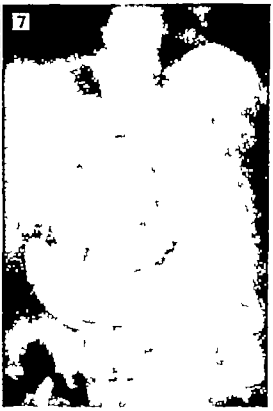
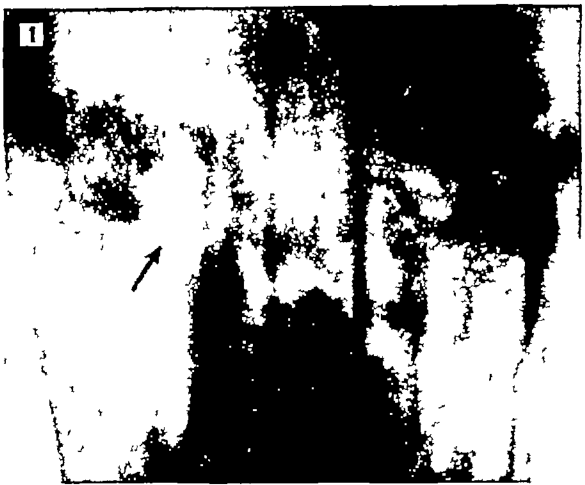
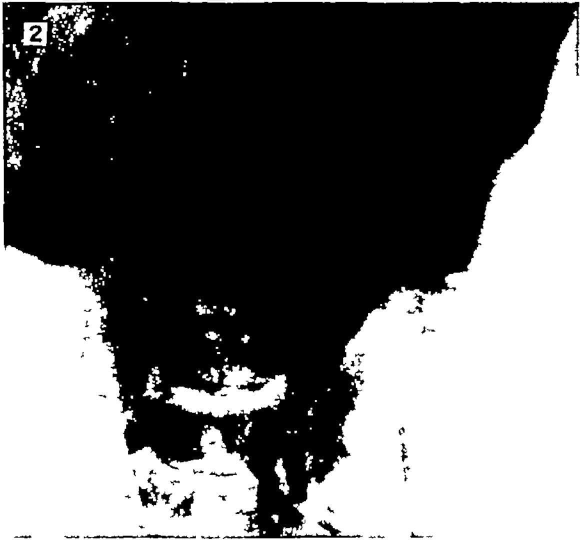
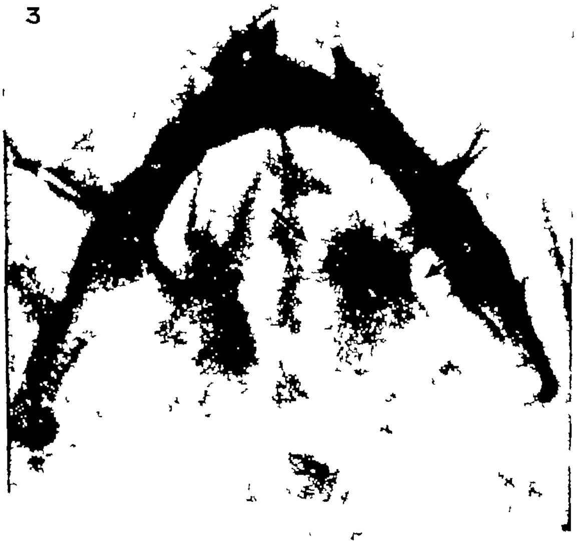


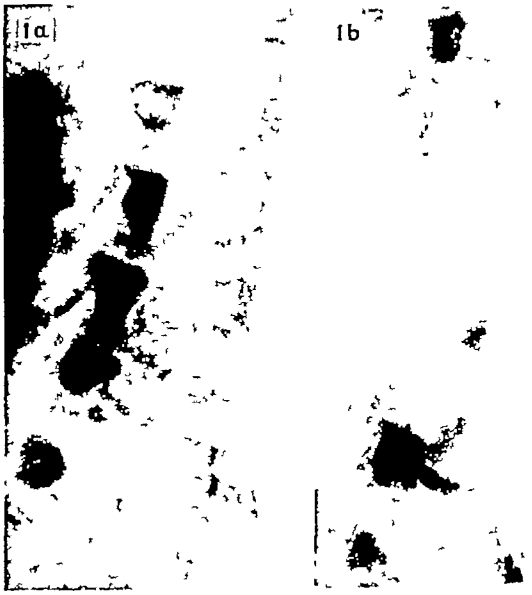
## DR HOLESH TUMOURS OF THE GLOMUS JUGULARE



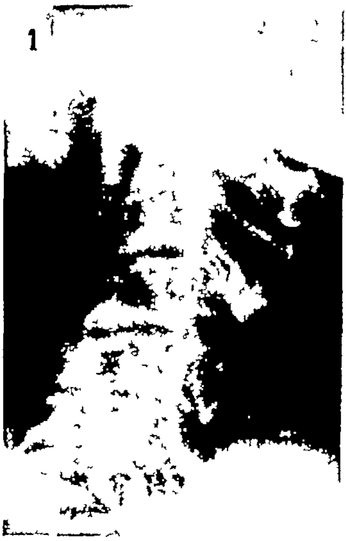


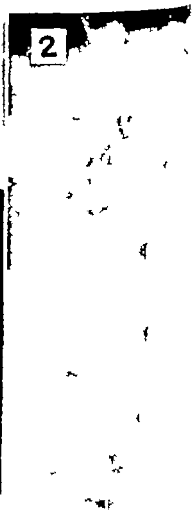


## PROFESSOR CAVE AND OTHERS OSTEO ARTHRITIS OF LUSCHKA JOI

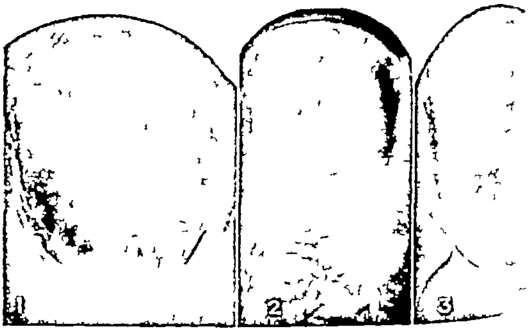


## DR CLARKE CERVICAL MYELOPAT





## DR TERRY ONYCHODERMAL BA



5 partial gastrectomies were done (table II) There e no deaths, and the striking features of these cases s the ease of the operation and the smooth post ative course (apart from 1 patient who developed umonia)

### Comparison of the Three Methods

n comparing the methods we must consider in order of ortance the number of deaths, the complications the difficulties.

*ths*

he deaths can be considered in three groups (1) re all the cases subjected to a particular method are uded without regard to the state of the patient on nission (2) the deaths which occurred with a icular method despite the fact that the patient was onably fit on admission and might have been expected urvive and (3) the deaths among patients who were n admission either from shock in the early cases or n infective peritonitis in the late

rom the present series (table II) and from the iously published cases (table IV) the following figures rge

|  | *Deaths among all admissions* |  |  | *Deaths which took place when recovery might have been expected* |  |  |
|---|---|---|---|---|---|---|
|  | *Cases* | *Deaths* |  | *Cases* | *Deaths* |  |
| -operative method | 466 | 36 | (7.7%) | 466 | 12 | (2.6%) |
| le suture | 1068 | 75 | (7.0%) | 633 | 15 | (2.4%) |
| ediate partial strectomy | 1225 | 97 | (7.9%) | 202 | 5 | (2.5%) |

he small numbers in the simple-suture and gastrec y groups where unexpected deaths are considered npared with the total numbers reported are due to fact that in many reports details of the deaths are given.

he patients who were gravely ill on admission were ally treated conservatively (the forced conserva method) Table III shows that of 50 such patients died These figures do not include the patients who e ill from cardiac failure bronchitis &c, but only se who were in poor shape from their abdominal istrophe.

he collected figures show therefore, that the mortality i whole and the mortality in reasonably fit patients do not differ appreciably whatever treatment is used but that for ill patients the conservative method is lethal. Finally, almost all published series show that the mortality of gastric ulcers whether treated conservatively or by simple suture is many times greater than that of duodenal ulcers

*Complications*

The complications can be considered as immediate and remote Table IV shows that the serious immediate complications of aspiration treatment—such as intra peritoneal abscesses—were 26 in 442 cases (5.9%) whereas in simple suture cases there were 59 in 607 cases (9.7%) In addition the 607 simple suture cases showed 105 (17.3%) lesser complications—such as wound sepsis and chest troubles—which did not occur in the con servative cases making a total of 27% No immediate complications are reported in the partial gastrectomy series but no doubt there were some although the writers emphasise the smooth postoperative course

As regards remote complications and troubles, collected series show that about half the patients who perforate will have subsequent severe symptoms (Sallick 1936, Estes and Bennett 1944 Illingworth et al. 1946 Forty 1946 Chamberlain 1951 Tandberg 1950 Lassen 1952 Gilmour 1953 Armitage 1954) It has also been shown that patients whose symptoms recur are usually those with a previous dyspeptic history (Illingworth et al 1946 Gilmour 1953), and Lowdon (1952) showed histologically that a long history is likely to indicate a chronic ulcer Finally Doll (1950) found 8.1% of 86 perforated gastric ulcers in men to be carcinomatous within three years

It therefore seems that as regards immediate compli cations simple suture is to be avoided As regards remote morbidity it seems equally clear that a long history of dyspepsia almost certainly means a recurrence of symp toms after the perforation is healed—and that a gastric ulcer is immediately and remotely dangerous

*Difficulties*

Simple suture is familiar to everyone and needs no further mention.

Aspiration is often spoken of as time-consuming and worrying It is no more time consuming than a laparo tomy but it does mean that the surgeon must be readily available in case of difficulties

Partial gastrectomy takes more time and may be impracticable for that reason

Finally if the surgeon is experienced and has a good anæsthetist he can choose his method at will If not he would be wise to avoid any operation

### Choice of Method

Patients may be divided into three groups:

(1) Those who are reasonably fit on admission—i.e. not shocked without obvious infective peritonitis and medically sound

(2) Those who are ill from the effects of the perforation

(3) Those who are ill from an associated medical condition

For patients who are reasonably fit on admission mortality is about the same for each method, and the choice of method should therefore depend on the morbidity immediate or remote As immediate compli cations are commoner with simple suture than with aspiration aspiration should be preferred to suture As between aspiration and gastrectomy aspiration is preferable for patients with a duodenal ulcer who have no history of dyspepsia or only a short history and who are therefore likely to remain symptom free after the perforation But in patients with a long ulcer history any treatment which leaves the ulcer in place will be followed by a recurrence of severe symptoms and this can be prevented only by immediate partial gastrectomy Finally gastric ulcers treated either by aspiration or by suture have a high mortality compared with duodenal

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## LEGENDS TO ILLUSTRATIONS ON PLATE

### DR. HOLESH

**1—Tomograph showing the characteristic erosion of the apex of e petrous bone.**

**2—Carotid arteriogram showing the complex arteriovenous astomoses at the base of the skull and neck.**

**3—View of the base of the skull showing the nasopharyngeal part a large glomus tumour**

### DR. CLARKE

**1 (case 1)—Myelogram; lateral view head down. Neck in full tension showing complete block at C5–6.**

**2—The same with neck flexed Radio-opaque material now passes e obstruction revealing filling defects.**

### PROFESSOR CAVE AND OTHERS

**1—(a) Normal cervical spine showing the capacious intervertebral ramina; (b) Luschka-joint osteo-arthritis showing protrusions of ophyseal osteophytes into four intervertebral foramina.**

### DR TERRY

**1—Opaque onychodermal band in patient with thyrotoxicosis.**

**2—Finger-nail of patient with hepatic cirrhosis showing both acity of the main pink zone ("white nails") and opaque onycho rmal bands. (N.B. The longitudinal flaw interferes with the white nail" but not with the opaque band.)**

**3—Opaque onychodermal band associated with local desquamation llowing paronychia.**

ulcers, and many prove to be carcinomatous Hence immediate partial gastrectomy should be done for these also They can be diagnosed preoperatively by the radiological method described below

The patients who are ill on admission from the effects of the perforation are usually, though not always, the late perforations It seems evident that partial gastrectomy is not to be considered (Even Nuboer (1951), who does partial gastrectomy as a routine, had 3 patients whom he considered too ill for operation ) As already stated, I believe that simple suture, toilet of the peritoneum, and *vigorous* supportive measures offer the best chance of survival

Lastly there are the patients who are ill on admission from an associated medical condition such as cardiac failure or severe bronchitis I cannot produce figures to support my opinion , but it seems reasonable in these cases to avoid the added strain of an operation and anæsthetic Aspiration is therefore likely to give the best results

### CONCLUSIONS IN BRIEF

Fit patients with either a long ulcer history or a gastric ulcer should be treated by immediate partial gastrectomy

Fit patients with a very short previous history of dyspepsia, or no previous history, should be treated by aspiration

Patients ill from the effects of the perforation should be treated by simple suture, toilet of the peritoneum, and vigorous supportive measures

Patients ill from an associated medical condition should be treated by aspiration

## Radiological Diagnosis of Site and Size of Perforated Peptic Ulcer

### *Method*

On admission the patient is treated in the usual way , but, instead of plain radiography of the diaphragmatic region for gas, 30 ml of viscous diodone (' Viskiosol six ') and 30 ml of sterile water, or 40 ml of 35% diodone, is squirted down the suction-tube, or drunk Three radiographs are then taken (1) with the patient erect (this is developed and viewed to see whether the exposure is correct, which takes about 10 minutes) , a second with the patient erect , and the third (immediately after the second) with the patient supine

Gastric suction is, of course, stopped while this is being done

### *Results*

57 patients have been radiographed in this way—19 with no stomach lesion, and 38 with a perforated peptic ulcer

Of the patients with a perforation, 22 were operated on and 16 were treated by aspiration The operated cases consisted of 19 duodenal ulcers, 2 prepyloric ulcers, and 1 gastric ulcer The aspiration cases were probably all duodenal, but so far only 9 have been proved by radiography after a barium meal

The stomach was surprisingly well outlined in all cases (figs 2–8) When the patient was well and without abdominal pain (e g , in routine outpatient radiography) the diodone passed rapidly into the duodenum and jejunum (fig 6) , but of 48 cases in which there was acute abdominal pain the diodone passed out of the stomach in only 14—i e , there seemed to be a pyloric spasm in most of these cases (figs 2, 4, 5)

Among the 22 patients with perforation who were treated by operation and in whom the diagnosis was therefore confirmed, there were 19 with duodenal ulcer, and in only 6 of these had the medium passed into the duodenum In 2 of these the films had shown escape of diodone through the perforation (figs 3 and 7) In the 13 cases, in which the diodone was retained in the stomach (fig 2), the duodenal perforation could not of [illegible] demonstrated The first prepyloric ulcer had in it a tiny perforation only, and no medium into either the peritoneum or the duodenum second perforation, with a diameter of 0 5 cm., an escape of diodone and was diagnosed preop (fig 4) In the case of the gastric ulcer a large seen (fig 5)

In 7 of the 16 perforations radiographed operated on, the medium passed into the 4 of these showed the viskiosol escaping duodenal hole (fig 8) , in the other 9 the pylorus to be in spasm (fig 2)

### DISCUSSION

Diodone and viscous diodone are used because water-soluble and soon absorbed Diodone is used for urography, arteriography, &c , and is and it has been injected into the peritoneum of the pelvis in doses of 20–30 ml without harm graphy ") (Kjellberg 1942, Jefferiss and Samuel It is possible that the polyvinyl alcohol in the diodone might cause some local reaction, becau only slowly absorbed , but the amount which through the perforation is very small—much than the amounts injected into the pelvis in graphy, which causes no reactions (Bergin 1951)

This method has not yet been used in enoug one to assess its value either in perforations or cases , but a good outline of the stomach is so obtained that one should be able to diagnose ulcers with reasonable certainty Duodenal p will occasionally be demonstrated but a negative has no value A minor use is to show wh stomach is full or empty after what appeared adequate suction

## Summary

An account is given of the treatment by one of 125 acutely perforated peptic ulcers 65 by asp 45 by simple suture, and 15 by partial gastrectom

A method is described of outlining the stoma demonstrating the site of the perforation radiolog

The three methods of treatment in the present and in previously published series are comp regards mortality, morbidity, and difficulties.

In patients who are in good condition on adm

(1) The mortality is the same whatever method

(2) The immediate morbidity of simple suture higher than that of aspiration

(3) The likelihood of recurrent or persistent ulc is very great in those with a long previous hist dyspepsia

Fit patients should undergo immediate partial tomy if they have a long previous dyspeptic h but if they have had little or no previous dyspeps should be treated by aspiration

Patients who are ill on admission from the ef the perforation will die if treated by aspiration gastrectomy The ulcer should be sutured and should be given *vigorous* resuscitative treatment

Those who, on admission, are ill from an as medical condition should be treated by aspiration.

It gives me pleasure to thank the surgeons at the Infirmary at Leeds for the opportunity to treat these and to publish the results , and Prof. A S Johnston staff for facilities, help, and coöperation in the radi studies

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# DIAGNOSIS OF MOURS OF THE GLOMUS JUGULARE

S Holesh

M.B Cape Town, D M.R.D  F F.R

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*With illustrations on plate*

MOURS of the glomus jugulare, once thought to be are now being reported with increasing frequency number published to date is approximately 84, but may well be more because some cases previously ded under different names are now thought to be us tumours

out half of these tumours arise in the adventitia e dome of the jugular bulb and then extend through loor of the middle ear into the tympanic cavity emainder originate from a glomus body within the oral bone Irrespective of the point of origin the ur may spread in one of two ways :

Progressive expansion in the middle ear with bulging drum which is destroyed and a granular mass then udes into the external canal.

The tumour extends medially along the petrous pyramid nscribing the labyrinth and eventually invades the l cavity with compression of central nervous structures involvement of one or more cranial nerves. These ent modes of extension account for the varying ptomatology

e tumour morphologically resembles the carotid paraganglioma and the two lesions may occur in ame patient Histologically the cells are large and gonal, with slightly eosinophilic cytoplasm and they to be uniform in size and shape They are arranged veoli or columns separated by a varying amount of na which is often very vascular Tamari et al ) consider that the adventitia of the jugular bulb is hly undifferentiated mesodermal layer and that any undergoing division here may become either a fibro a histiocyte or an endothelial cell On this basis ours arising from the glomus jugulare may vary in gross structure tendency to hæmorrhage rate of th and response to radiation therapy This also ins the confusing nomenclature

cept in children, the tumours grow very slowly and may reach an advanced stage with intracranial sion before they are identified. The duration of toms before the patient seeks attention varies from months to twenty years The length of illness may wenty to thirty years. 15–20% of cases become gnant after a long benign course Metastases have been reported in the liver, lungs, and cervical glands in a few cases

Several deaths have been recorded up to 1951 : 2 occurred after attempted removal of the tumour, 4 as a result of gross intracranial extension, and 1 following meningitis and a cerebellar abscess

The majority of patients are middle-aged females who usually present with aural symptoms A definite familial tendency has been described

## Symptoms and Signs

The commonest symptoms are chronic otorrhœa progressive deafness, tinnitus, and hæmorrhage from the affected ear especially on manipulation of a polyp which is often present If only a superficial portion of a polyp has been removed for biopsy the true diagnosis may be missed and obviously not all aural polyps are examined histologically A bruit over the mastoid area and neck is occasionally the presenting or dominant symptom

As the tumour spreads neurological disturbances occur multiple cranial palsies being characteristic The cranial nerves most frequently involved are the 7th 8th 9th 10th 11th and 12th The 5th and 6th nerves are occasionally affected Trigeminal pain or sensory disturbance may arise from local pressure without actual involvement of the nerve Ataxia and nystagmus have been described but pyramidal signs are uncommon Sensory disorders and symptoms of increased intracranial pressure are also rare

Although few present with neurological symptoms 40% of the reported cases had clinical evidence of some neurological disturbance such as hoarseness due to involvement of the vagus The earliest neurological symptoms described have been dryness or stiffness of the tongue a sensation of irritation in the pharynx dysphagia and aphonia Headaches, vomiting and failure of vision were the only manifestations in the cases recorded by Dockerty et al (1951) Hierons (1954) described a case presenting with papillœdema.

## Radiological Findings

At some stage during the disease the radiological appearances are often diagnostic but surprisingly enough there are only two radiological papers on this subject (Cova and Meda 1952 Riemenschneider et al 1953) The radiological signs are

(1) Sclerosis of the mastoid which cannot be differentiated from a chronically infected mastoid without tomography

(2) Destruction of the lower portion of the petrous pyramid the ridge remaining as a more or less intact shell (fig 1) The type of erosion peculiar to glomus tumours can only be demonstrated satisfactorily by tomography—a very simple procedure in this area.

(3) Enlargement of the jugular foramen on the affected side with perhaps a mass in the posterior nasopharynx (fig 3)

(4) On arteriography a tortuous mass of new vessels in the neck the petrotemporal region, or posterior fossa (fig. 2) (Alexander et al. (1951) think that the early blood supply of the tumour is from the external carotid artery and later also from the vertebral artery and they state that the tumours are best seen in the venous phase of the arteriogram.)

(5) Signs of raised intracranial pressure such as thinning and destruction of the clinoids when the tumour has extended widely into the middle and posterior fossa.

## Differential Diagnosis

Destruction of the base of the skull including the petrous bone may be seen in the following diseases but the erosion in glomus tumours differs in its site of origin and other features

(1) *Acoustic neuroma.*—There is less emphasis on the massive destruction of the lower portion of the petrous pyramid a the widening and erosion is chiefly of the internal audi meatus No soft tissue mass is seen in the na

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MR MOORE: REFERENCES—*continued*

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(2) *Primary tumours of the nasopharynx* may erode the base of the skull but massive destruction of the entire petrous pyramid is most unusual

(3) *Chordomas*—Destruction of the dorsum sella occurs first and may extend to involve the petrous bone at a later stage The erosion of the sella is much more extensive in chordoma and there may be much calcification in the tumour

(4) *Carcinoma* of the sphenoidal sinus will show its primary destruction locally

(5) *Metastatic carcinoma* may present a similar picture to the glomus tumour

The vascularity of the glomus tumour as seen on angiograms is never a feature of these lesions, and this, coupled with the tomographic findings, clinches the diagnosis

## Illustrative Cases

The following 5 cases, seen at the Westminster Hospital, show many of the characteristic radiological findings

**Case 1**—A woman of 52 had had hoarseness for nine years when her *doctor noticed "something wrong with her tongue"* Vertigo set in eighteen months ago, and painless bleeding and purulent left otorrhœa have been present for about nine months During the past four months a squint developed with double vision on looking to the left There was paralysis of the left 5th, 6th, 7th, 8th, 10th, 11th, and 12th nerves An offensive left otorrhœa was present and a tough polyp, which bled readily on manipulation, was obstructing the left external auditory meatus There was a systolic murmur over the left mastoid extending down the neck X ray examination showed a sclerotic left mastoid with erosion of the apex of the petrous bone, the extent of the erosion was well demonstrated by tomography The left jugular foramen was enlarged A left carotid arteriogram (fig 2) showed a very vascular tumour at the base of the skull There was free communication between the carotid arteries and jugular veins The cerebral vessels were poorly filled owing to the extent of the shunt A biopsy of the aural tumour showed the typical appearances of the glomus tumour Following a course of *radiotherapy*, to a total tumour dose of 5600r, the local condition in the ear improved considerably, but *no objective change has occurred* in the neurological signs

**Case 2**—A woman of 38 had a left cortical mastoidectomy twenty years ago, followed by a radical mastoidectomy in 1941 She had no symptoms until 1948, when bleeding *occurred from the left ear Further exploration of the left* mastoid was followed by facial palsy of four months' duration

There were no further symptoms until 1951 when the left facial palsy recurred with slight hoarseness When seen in 1953 there was a left 7th nerve palsy and partial paralysis of the 5th, 6th, 9th, and 10th cranial nerves A vascular tumour was found in the left ear and biopsy confirmed the diagnosis of a glomus tuomur Tomographs showed typical destruction of the apex of the left petrous Following a course of X ray therapy (maximum tumour dose 4900r), there has been no change in the neurological signs

**Case 3**—A woman of 72 had symptoms dating back to 1939 when she had sudden weakness in the arms and legs In 1943 her tongue had become "one sided," and in 1944 she developed dysphagia and right facial weakness with a tendency to fall to the right on walking At that time there was nystagmus, partial palsy of the right 5th nerve, and complete palsy of the 7th, 8th, 9th, 10th, 11th, and 12th nerves Sensory ataxia and diminished vibration sense were also present, and a diagnosis of syringobulbia was made In 1945 new vessels were noted on the right ear drum and she complained of headaches giddiness, dysphagia, and dyspnœa Her B.P was 230/120 In 1948 she developed diplopia and because of the increase in the vascularity of the ear-drum, a hæmangioma of the tympanic membrane was diagnosed Erosion of the right petrous was first seen in 1949 and has not altered (fig 1) On her last admission a 'cherry red tumour' was seen protruding from the right ear drum which is characteristic of a glomus tumour Teleradiotherapy was started in 1945 and she has had two further courses The signs and symptoms remain unaltered

**C**  **4**—A man of 59 was admitted in 1954 with a history and pain in the right eye since September, 1947 was right proptosis and complete right 6th nerve palsy Radiographs of the skull and a right carotid arte were normal There was no abnormality in the nas or ears In 1949 hoarseness and dysphagia later slight weakness of the right arm There were of the 6th, 9th, 10th, and 11th nerves, and right deafness Tomography showed a nasopharyngeal m destruction of the right petrous and posterior clino 1950 the dysphagia had increased, and the left nerves became involved to a greater extent The sy improved after a course of radiotherapy He reasonably well and returned to work in February Sub X ray examination showed calcification above the an increase in the destruction at the base of the skull to involve the right wing of sphenoid and optic recent right carotid arteriogram showed elevation carotid siphon and straightening and stretching of the carotid in the anteroposterior view No abnormal ves seen at the site of the tumour

**Case 5**—A man of 55 was admitted to hospital with a left squint, which had been present since 19 operations on this eye in 1951 and 1952 On examina were palsies of the left 5th and 6th cranial nerves, constriction of the left visual field, and a dimini corneal reflex Deafness in the left ear had set in There was extensive destruction at the base of the erosion of the left anterior and posterior clinoids and tion above the petrous Tomography demonstrated tion of the apex of the left petrous bone as well as of the mastoid antrum A left carotid arteriogram displacement of the internal carotid and middle arteries

## Summary and Conclusions

A tumour of the glomus jugulare should be co if there is a long history of increasing unilateral a hæmorrhagic otorrhœa, or a vascular polyp in t If an apparently simple chronic otorrhœa is with unusual neurological signs, tomograph petrous bone will show characteristic findings graphy in the anteroposterior projection is m reliable than the conventional views of the petr and should be carried out in all suspicious cases arteriography is not indicated if, as so often happ diagnosis can be made on the clinical and tom findings

Of the 5 cases described here, 2 are proven histol and 1 has all the characteristic clinical and radi findings The other 2 cases (4 and 5) are probable tumours in view of the long clinical history, rel benign course, multiple cranial palsies, and charac tomographic appearances

I am indebted to Dr F M Allchin, Mr D Walker Dr Peter Kerley, and Dr S P Meadows for perm publish these cases

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# CERVICAL MYELOPATHY

## A COMMON NEUROLOGICAL DISORDER

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*With illustrations on plate*

EGENERATION of the spine occurred in prehistoric ,als as well as in primitive man (Moodie 1923) and ges in the cervical region—now known collectively cervical spondylosis [1]* (Schmorl and Junghanns )—have been found in the ancient Egyptians fer and Riotti 1912) It is well known that cervical involvement is more common in the elderly and lendahl and Kunert (1954) report radiological evi e in 75% of persons between 50 and 75 years of age vitz (1940) and Morton (1950) found a similar inci o among cadavers and it follows that as the average of the population increases it will become even more ıent Nevertheless younger age-groups are not 'ely exempt (Hult 1954 Kuhlendahl and Kunert )

e possible clinical significance of these findings has ver only recently been recognised Involvement of pinal roots (see Frykholm 1951) is now an accepted l but the effects upon the spinal cord (Masson and e 1949 Brain et al 1952 Spillane and Lloyd 1951 Müller 1951 and others) are less well known proposed to deal only with this latter type of case and as the pathology of the condition is still ure the term cervical myelopathy —also used by (1954a)—is employed.

spite its recent publicity our knowledge of this se is still incomplete and our conceptions of it times inaccurate Thus it is often thought of as ly a surgical entity (Bucy et al 1948 Allen 1952 and Temple 1953 Semmes and Murphey 1954) ly simulating certain degenerative and frequently atable diseases of the nervous system (Jager and e 1949 Strully et al 1951 Liversedge et al 1953) e cases, however are only part of a syndrome the s of which have not yet been defined

has recently become apparent that cervical myelo y in its various degrees is a much more common der than is at the moment generally supposed and the clinical spectrum is much wider In addition ems likely that certain hitherto unexplained neuro al signs found occasionally in the elderly may be to cervical spondylosis The purpose of this paper present and evaluate cases of cervical myelopathy ved over a period of fifteen months in an attempt to tantiate these assumptions

### Classification of Material

e 32 cases of cervical spondylosis with spinal cord lications that form the basis of this report can be eniently divided into groups according to the severity e clinical picture

up I (15 cases) —All of these patients complained of le with their legs or arms or both They had the clinical gs usually associated with cervical myelopathy (Brain 1952)

up II (12 cases) —These patients had symptoms of al root irritation only but on examination evidence of compression was found

up III (3 cases) —Here neurological abnormalities were vered but no accompanying symptoms could be elicited

up IV (6 cases) —It was on occasion thought that cer myelopathy was complicating other diseases either of the nervous or other systems. 4 of the cases have already been included in groups I and II

#### GROUP I

Of the 15 patients in this group the diagnosis has been verified at necropsy in 1 (case 2) and by myelo graphy in 11 7 of the latter have been included in a review of this disorder (Clarke and Robinson) The 3 in which myelography could not be carried out because of the patients wishes or age had adequate radiological evidence of cervical spondylosis and their clinical states corresponded exactly with what is becoming accepted as characteristic of the disease

Because we have only recently become aware of cervical myelopathy as a common condition its clinical variations and in particular the early stages are not well known The cases here presented however give some indication of the degree of variation to be expected among this group of patients

The most severe type of case is represented by 4 patients They were all severely paraplegic and 3 had symptoms also in their upper extremities Of the latter the following is typical

**Case 1** —A retired postman aged 60 said that four or five years ago he had noticed cramps and aching in the calves, followed by a weakness of the right foot three years before admission to hospital Eighteen months before admission after a period of bed rest the whole right leg became weak and soon the left was similarly affected His walking deteriorated progressively until he was bedridden Two years before admission he had weakness and paræsthesiæ in the ulnar two fingers of the right hand which spread to the whole hand and arm. The same symptoms had appeared in the left hand Sphincter functions were normal and he had never had any neck symptoms.

Forty five years previously he had fallen and fractured the left clavicle but suffered no apparent sequelæ

*Examination* —He was a small poorly developed man con fined to his bed The neck was normal apart from slight painless limitation of movement in all directions except flexion Wasting was generalised in the limbs but more marked distally and coarse fasciculations could be seen in several muscles. Tone was increased in all limbs but more so in the lower extremities and more on the right side Wrist and finger extension and dorsiflexion of the foot on the right were impossible and extension of the forearm and flexion of the thigh on this side was severely affected. Weakness of a similar distribution but less severe was found on the left side The triceps jerks were absent and brisk finger flexion accompanied the biceps and supinator reflexes the finger jerks were exaggerated The abdominal reflexes were absent and those in the lower limbs much increased plantar responses were extensor Slight pain and temperature impairment could be demonstrated on the left and posterior-column modalities were decreased more on the right side and more in the legs

*Investigations* —Cervical-spine X ray : a marked lordosis centring on C6 with acute angulation forward of the spinal canal The body of C6 was wedge shaped and those of C3 C4 and C5 were distorted by gross degenerative changes (fig 1) Cerebrospinal fluid (C.S.F.): manometry performed in the usual manner showed no obstruction but with the neck in full extension a complete block could be demonstrated The fluid s contents were normal Myelogram with the neck in extension there was a complete hold up of the radio-opaque material at the level of C5-6 (fig 1) and only repeated neck flexion would allow it to pass (fig 2) There was also partial obstruction at the C4-5 and C3 4 level

*Treatment and Progress* —The patient has been provided with a plastic collar and a spring splint for the right fingers Intensive physiotherapy has produced slight improvement It is not however expected that recovery will be extensive at this stage of his disease ; surgery was not con idered po sibl

A diagnosis of ? motor neurone disease had been made elsewhere but there was clear clinical evidence of a focal cervical lesion which was located by myelograp s It is possible that the sixth cervical vertebral b damaged by the fall and the r sultant instal encouraged the excessive degenerative ch played by his occupation can only be presumptive, but for many years he had carried a postman's bag on his left shoulder His spinal cord has little or no reserve of function , for, as soon as inactivity is enforced deterioration occurs Thus, a recent pulmonary infection has undone the previous progress

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[1] hough the primary defect is in the intervertebral disc other ctors are present and in the type of case to be described term u h as prolapsed disc should be abandoned

At the other extreme of the clinical spectrum is case 2

**Case 2** —A caretaker, aged 62, had an attack of bronchitis, to which he was subject, four months before admission to hospital On resuming work a month later, he noticed a mild weakness of the left foot so that it would drag after he had been walking for about ten minutes There were no other symptoms

*Examination* —The signs of aortic regurgitation were found and the blood pressure was 200/100 There was moderate weakness of the dorsiflexors of the left toe and foot The reflexes were increased in the left arm and leg, with an extensor plantar response on that side

*Investigations* —Cervical spine X ray severe degenerative changes especially at C5–6 and C6–7 levels C S F contents were normal and there was no block, with the neck in the neutral position

*Progress* —A month after discharge, he was readmitted in congestive cardiac failure and died the same day

*Necropsy* —Rheumatic aortic valvular disease and gross pulmonary œdema were present On the anterior wall of the cervical spinal canal and almost entirely on the left side, was an osteophytic excrescence at the disc space of C5–6 The spinal cord had been indented by it and by smaller protrusions at other levels Appropriate staining showed degeneration in the left lateral column

In patients with the more advanced disease it is not unusual to find that the first symptom was, as in this case, a weakness of one lower limb, and that over a period of months or years other extremities were involved until the full picture was produced (cf case 1)

Although many examples of cervical myelopathy similar to case 1 have been described, those with milder changes have been given less notice The following is a second instance of the latter type

**Case 3** —A male ballet-dancer, aged 39, had noticed wasting of the right hand and pain in the right shoulder for eight months Neck movements provoked the pain, and in addition he experienced paræsthesiæ in the right thumb, index, and middle fingers For a similar length of time the left leg had felt " dull " and he was less agile on it than previously

*Examination* —Lateral flexion of the neck to the right produced pain There was moderate wasting and weakness of the small muscles of the right hand and slight weakness of the triceps on that side The right triceps jerk was absent and the left knee jerk brisker than the right , the left plantar response was extensor Tactile and painful sensibility were impaired over the right thumb, index, and middle fingers

*Investigations* —Cervical spine X ray moderately severe degenerative changes at C6–7, especially on the right side C.S F (examined elsewhere) no block and contents normal Myelogram " a filling defect at the C6 level "

*Treatment and Progress* —He is still under treatment and is having intermittent neck traction and local physiotherapy to the neck and right shoulder He is relieved of the pain but the signs still persist and weakness of the left leg is unchanged.

It seems probable that this man has noticed the symptoms of cervical myelopathy early because he is observant and depends on his limbs for the execution of skilled and delicate movements Thus it is only when he is dancing that he notices a defect in the left leg , it is not noticed at other times He is the youngest patient in the whole series and it is likely that trauma has played some part in his case , his symptoms began after vigorous dancing It is unusual to find root symptoms in an upper extremity and cord symptoms in the contralateral leg More usually the root and cord symptoms are on the same side (cf cases in group II) As, however, there are often multiple cord compressing lesions in this condition, considerable variation is to be expected

[illegible] remaining 12 cases in group I are intermediate as [illegible] severity between case 1 at the one extreme and cases 2 and 3 at the other Dysphagia due t anterior osteophytes (Bauer 1953) was encoun only 1 case In 9 of the 15 cases, a diagnosis of myelopathy was made either here or elsewhere diagnosis had been propounded in each of the cases but further investigations revealed the corr Thus 3 of the patients were thought to be suffe disseminated sclerosis, 1 from syringomyelia, 1 spinal arachnoiditis, 1 from an intramedullary cord tumour, and 1 (case 1) from motor-neurone It can be stated, however, that when the picture of cervical myelopathy is adequately clinical confusion with other diseases should not

### GROUP II

The 12 patients in this group had the feat cervical root irritation but spinal cord signs (u or bilateral) could be demonstrated though th not associated with any symptoms These ca similar to those spoken of by Stookey (1940) as to " the syndrome of unilateral ventral pressure pathological lesion being a combination of root compression It should, however, be noted that th not necessarily exist at the same level, as Stooke believed

All the patients presented themselves at hosp the clinical picture of cervical root irritation, the of which have been adequately dealt with m papers (see Frykholm 1951) No estimate of incidence of these cases is possible, but during th period in which the 12 cases were observed instances of root compression without these featu encountered

The ages of the patients did not vary sig from those in group I, which is of some interest considers that cases of root compression due to losis tend to occur at an earlier age than cervical myelopathy Every patient had referable to the neck The cord signs varied but they were all mild and invariably motor sensory disorders of definite cord origin were not This is in keeping with the known susceptibility pyramidal tracts to compression, recently experimentally by Tarlov (1954) In only 1 case a contralateral extensor plantar response and is th a link with *group* I (cf case 3) 3 patients had cord signs but in the remainder they were The former included 2 cases with bilateral plantar reflexes as the only indication of cord and in 1 of these myelography confirmed the di The 3rd case is typical of this subgroup

**Case 4** —A bus driver, aged 49, had suffered pain shoulder for three years and clumsiness of the left six months He had complained of a sensation of num the left thumb for four months and the shoulder extended to this digit The lower limbs were norm

*Examination* —Neck movements to the left produ The left triceps and thigh flexors were slightly weak lations were occasionally present in the left deltoi supinator reflexes were both inverted and the fin much increased Thigh flexors were slightly weak reflexes were brisker on the left , both plantar re extensor The only sensory impairment was in the ter the left C6 root

*Investigations* —Cervical spine X rays degen changes more marked on the left C.S.F complet with neck in full extension contents normal My complete block at C4–5 with the neck in extension

*Progress* —Heat and massage to the neck and left produced gradual improvement Neck traction did any relief He now has only mild neck pain and for nine months has been able to drive his bus

In this case there is clear evidence of cord co yet there are no symptoms referable to it improved with conservative treatment but is under vation because of the chances of deterioration in yelopathy

the 9 patients with ipsilateral cord signs 6 had sed tendon jerks only in nearly every case these onfined to the lower limbs and they might or might e accompanied by extensor plantar responses and ised abdominal reflexes on that side Why hyper ia should sometimes occur without an accompanying logical plantar reflex remains unexplained In 2 slight hypertonicity existed in the ipsilateral forearm se 5 is one of them

e 5 —A housewife of 62 had experienced severe burning ooting pain in the right hand for five weeks It affected ddle finger mostly and was worse when in bed at night ion was impaired in the hand For a similar length of here had been stiffness of the neck and pain extending t into the right shoulder

*mination* —Neck movements were limited by pain was slightly increased in the right forearm but apart xaggerated tendon jerks and an extensor plantar reflex right the rest of the nervous system was normal

*stigations* —Cervical-spine X rays spondylotic changes 6 level.

*tment and Progress* —Local palliative measures have ed complete freedom from the previous symptoms for onths.

s patient was referred as a case of the carpal tunnel ome However the cord signs the neck symptoms, ative cuff test (Gilliatt and Wilson 1953) and the se to treatment directed proximally make that osis unlikely It also seems improbable that she is ing from two lesions a possibility that must be ered in some cases The finding of cord signs in of brachial neuritis" is obviously of considerable atic value

elographic evidence of the cervical lesion was only ed in 2 of the 12 cases, the other patients being in the outpatient department However the nation of cervical root irritation with cord signs, adiological evidence of spondylosis in all of them, ents a distinct syndrome

the moment the prognosis in these cases is wn but it is important to observe that although from root symptoms was achieved in most cases yelopathic signs persisted

## GROUP III

number of cases in each group does not necessarily the relative frequency of the types. Thus although are only 3 in group III these cases may be com r than any of the other types The patients, who all over 65 years of age, attended hospital for com s that were not related to the cervical spondylosis ered incidentally on X ray examination The ing is a typical example :

e 6 —An ex Army physical training instructor aged 66 ained of peculiar sensations in his knees and locking of ght elbow Five years previously he had suffered a attack of right sciatic pain

*mination* —Degenerative disease of the knee joints and osteo-arthritic changes in the right elbow accounted for mptoms However there were bilateral extensor plantar s slight impairment of joint position sense in the right e and decreased vibration sense appreciation in the parts of both lower limbs To clinical examination, the was normal

*tigations* —C rvical spine X rays gross spondylotic es maximal at C5–6 C.S.F no block with neck in exten or flexion contents normal Myelogram : moderate tation of the anterior surface of the Myodil column levels of the cervical spine but mostly at C5–6. There o block on extension A filling defect at the L4–5 level ited a prolapsed disc

*tment and Progress* —He has been treated with physio- py and is pursuing a fluctuating course closely related to f employment The abnormal signs are still present unchanged after twelve months observation

The previous attack of "sciatica" indicated a disc lesion in the lumbar region, verified by myelography That certain persons suffer from multiple disc lesions is now recognised (Brain 1954a), although some may be symptomless (Trowbridge and French 1954)

In the other 2 cases the clinical findings were much the same although in each there were reflex abnormalities in the upper as well as the lower extremities. One like case 6 had a mixture of mild motor (including slight muscle weakness) and sensory changes while the other had only motor impairment In each there was a hemiplegic distribution of the signs A lumbar puncture or a myelogram was carried out in each one of them and the findings were the same as in case 6 It is interesting to note that in this man severe cervical spondylosis prevented adequate neck extension and may therefore be protecting his spinal cord from further damage as was probably the case also in a patient belonging to group I

The cases comprising this group are included with much less certainty than any of the others However the recent study of Pallis et al (1954) and the myelographic evidence in 2 of the present cases help to confirm the existence of this clinical entity Pallis et al (1954) have investigated a group of non neurological patients over the age of 50 both clinically and radiologically They found that 60% had neurological abnormalities and all of these had cervical spondylosis As in the cases described above, the abnormal signs were mild symptomless, and either motor or sensory or both The fact that posterior osteophyte formation seen on lateral X ray examination of the cervical spine does not necessarily indicate narrowing of the spinal canal as maintained by these authors does not detract from the importance of their work. However the rôle of thoracic spondylosis (excluded in case 6 and the others) must also be considered Despite the presence of cervical spondylosis spinal-cord signs may be due to compression at a lower level

It should be noted that all the patients in group III were of limited intelligence and it is possible that they had not noticed certain disabilities that would be more readily discernible to more observant individuals

Another objection to attributing spurious neurological signs in the elderly to cervical myelopathy is the possibility of other lesions producing them. Savitsky and Madonick (1943) offer several suggestions to account for the extensor plantar reflexes in a healthy individual but the only one to be considered seriously is cerebral arteriosclerosis and associated mild cerebrovascular accidents those have been excluded as far as possible from the 3 cases of this group However this is a formidable consideration when dealing with patients over 65 At least 4 cases not included here in which this problem arose have been considered recently but in the absence of pathological studies a definite conclusion is not possible

## GROUP IV

If it is correct that cervical myelopathy is a common disorder it would not be surprising if it were found with other diseases This association has in fact been observed and group IV contains those patients in whom two pathological processes could be detected. It is convenient to consider first the occurrence of cervical myelopathy with non neurological conditions, and then the more difficult problem of two coexisting diseases of the nervous system

Cases belonging to the first type have already been included among the various groups of cervical myelopathy Thus in group I the second patient (case 2) was suffering also from aortic incompetence and died of congestive cardiac failure Another patient was admitted to hospital because of ischæmic heart-disease and was found to have the signs and symptoms of a C6-compressing lesion although she had not complained spontaneously of it Case 7 presented below is of particular interest because of the difficulty of differentiating between the two diseases

**Case 7** —A blacksmith, aged 49, was referred to Dr Russell Fraser as a case of thyrotoxic myopathy He had been losing weight for two or three months and for five weeks had noticed weakness of the legs, particularly the left one He was becoming tremulous and more excitable than usual

*Examination* —He was anxious and sweating There was generalised muscle wasting with coarse fasciculations in several groups and considerable associated weakness, more marked in the left triceps The reflexes were all abnormally brisk except the left triceps jerk which was almost absent, the plantar responses were extensor, the left being the more definite Auricular fibrillation was present, and, though the thyroid was not palpably enlarged, the patient was clinically thyrotoxic

*Investigations, Treatment, and Progress* —No C.S F block was demonstrated, but neck positioning was not employed, the protein content of the fluid was 90 mg per 100 ml Thyrotoxicosis was readily confirmed and the patient was treated with methyl thiouracil and *l* thyroxine Improvement was dramatic and when the thyrotoxic symptoms had disappeared, his only complaint was of some weakness of the left leg On re examination the only abnormalities were marked weakness of the left triceps and moderate involvement of the small muscle of the left hand the left triceps jerk was still absent and all the other reflexes were brisker than normal the plantar responses were still extensor

A manometric block with the neck in extension was now demonstrated The C S F protein content was still abnormal and X rays of the cervical spine revealed moderate changes at C5–6 and C6–7 A myelogram confirmed the block in extension the main compressing lesion being at C6–7

Now, three years after his first complaint began, his thyroid function is normal, but he still notices some weakness of his left leg

This man had severe muscle wasting associated with thyrotoxicosis and it was only after this had been treated that it was possible to evaluate the evidence of a focal cervical cord lesion No specific therapy has been directed at the latter, but he is being closely observed and deterioration will call for a further consideration of treatment

One case included in group II should also be mentioned here The patient, a man of 68, was admitted because of chronic bronchitis, and on examination was found to have severe wasting of the right shoulder girdle and biceps He stated that this had been present for about eight years He had the signs of a C5 root lesion on the right and also ipsilateral pyramidal-tract signs Neck movements especially extension, were restricted, and X rays of the cervical spine revealed marked degenerative changes at all levels In his occupation he had carried bags of coal on his shoulders

A man of 67 was suffering from diabetes mellitus but had mild pyramidal tract signs on the left side It was considered that he might be an example of diabetic myelopathy (Garland and Taverner 1953), but, in the presence of restricted neck movements, severe cervical spondylosis, and evidence elsewhere of root pain, it seems reasonable to suggest that spondylotic myelopathy may be playing a rôle in this case

It is also possible that cervical myelopathy may complicate neurological diseases, but here differentiation may be difficult or impossible Case 8 is an example of this subgroup

**Case 8** —A waitress, aged 43, for two or three years had experienced paræsthesiæ all over the right hand and to a lesser degree in the left A similar sensation, together with stiffness, had been present in the legs for about a year More recently there had been aching in the shoulders with extension to the left arm

*Examination* —She was tense and anxious but her general dition was good A coarse sustained nystagmus with l gaze to either side was found and sensation was ired over all of the left side of the face and tongue There an adductor palsy of the right vocal cord, the right side of the tongue was wasted, and active fibrillation seen The right upper limb was wasted and weak, par proximally, and the right thigh flexors were also affected All the tendon jerks were absent in the rig extremity, but in the left both the biceps and reflexes were entirely replaced by finger flexion and th and finger jerks were pathologically brisk on this side lower limbs the reflexes were increased (more so on t side) and both plantar responses were extensor P temperature sensation was impaired over the left the body and over the right shoulder, but the column modalities were affected mainly on the right principally in the hand

*Investigations* —Skull X ray no basilar Cervical spine X ray marked degenerative changes larly at the C5–6 level C S F a manometric block neck in full extension Myelogram a complete br myodil column at C5–6 level with the neck exten was therefore concluded that she had syringobul syringomyelia complicated by cervical myelopathy

*Treatment and Progress* —She was treated with therapy and a course of radiation therapy, and, althou has been little improvement in her condition, there h no deterioration over the last year

The arm reflexes indicated a focal cervical-cor and investigations showed that spondylosis was It is conceivable that patients with a cervical-cor are more likely to suffer from spondylotic c of the spinal canal because of the increased si spinal cord No attempt has been made to r compressing lesion, this will be considered if occurs The detection of this complication i im because it may be possible to relieve some sy despite the fact that the primary disease i influenced by therapy

## Discussion

Recognition of the clinical aspects of cervical losis is relatively recent One reason for the that, as Pallis et al (1954) point out, we have to believe that degenerative changes in the c spine are, like arteriosclerosis, an inevitable acc ment of the normal ageing process, as is shown tendency to describe them as "normal for the the patient" Another reason is that Schmorl associates (see Beadle 1931), when studying th vertebral disc, did not extend their investigat include the cervical spine A third is that it customary to attribute inexplicable neurological elderly persons to cerebral arteriosclerosis or t degenerative changes in the brain or spinal cord logical examination of the cord has usually been for those cases with clear evidence of a cord l information in other cases is thus incomplete

### *Incidence*

The cases included in this report were all se medical wards or in the outpatient departm general hospital It has not been found p estimate the true incidence of cervical myelop it is clear that in all its various forms it is o commonest neurological diseases encountered the same period of observation, about 40 ex uncomplicated cervical root involvement were as well as 2 cases of acute cervical cord lesion latter, 1 had a true disc prolapse and so was the cases described by Bucy et al (1948), and improvement followed operation In this was no history of neck trauma, but in the 2 frontal head injury had produced forceful hype of the neck Limb symptoms were absent but p tract signs of cervical cord origin were pres side This sequel to a head injury is well kno 1944), but it is one of the possible comp cervical spondylosis (Walshe and Ross 1936, B which was present in this patient Although t have cord lesions they have not been inclu

series because of their strict relationship to *acute*
.

### *y and Pathology*

out discussing the detailed pathological changes
cervical vertebræ (Frykholm 1951, Brain 1954a,
dahl and Kunert 1954) it is possible to suggest
pondylosis producing cervical cord compression
due to senile degenerative disc and bone changes
erefore "primary, or may be secondary ' and
ted with congenital anomalies of the cervical
ro or acute neck trauma The primary type
ts for the vast majority of cases and it seems
that chronic occupational trauma may be in part
sible in some of them (Hult 1954) Thus in 7 of
cases this possibility existed, 5 had habitually
heavy objects on their shoulders (4 in group I and
roup II) and 2 had been subjected to unusual
s (cases 3 and 6)
d secondary spondylosis—2 in group I and 1 in
II In the former the anomaly was single in one
nd involved only one lamina, but in the other
here were multiple bony lesions The group II
t had a congenital fusion of the bodies of C4 and
each of them spondylosis due to resultant mech
instability was in evidence and had produced the
sion The clinical pictures in the different types of
losis are indistinguishable and treatment is the

ætiology of the cord changes is still under dis
but the hypothesis of vascular insufficiency
l by Morton (1950) and Allen (1952) has been given
t by Mair and Druckman (1953) and Girard et al
although they do not agree on the actual mecha
This hypothesis would adequately explain the clini
lings in the present series although direct neuronal
e (Bedford et al 1952 Tarlov 1954) and arach
's (Girard et al 1954) may also play a part The
provides no direct evidence in favour of Taylor's
view that posterior as well as anterior compression
but the suggestion is a very plausible one

### *sis*

of the most important diagnostic features of these
s the reflexes. As was pointed out by Walshe and
(1936) the tendon jerks in the arms are of particular
ing value partial or complete inversion of the
and biceps, and a hyperactive finger jerk are
tly encountered
metry carried out with the neck in various posi
postural manometry ') is a valuable test (Kaplan
nnedy 1950) So far a 100% correlation has been
hed between the manometric findings and those
lography if the former demonstrated a block
er confirmed and localised it Furthermore in
s in group III a block was absent with both pos
anometry and myelography In figs 1 and 2 the
neck extension on the myodil column is shown
ealing with group I patients it may therefore
e be possible to dispense with myelography
al radiological and manometric findings are
This will be of value if the patient is frail or
therapy is not contemplated Experience indi
t the test is of less value in cases with evidence
r cord involvement (groups II and III) Con
of the findings of Pallis et al (1954) will
facilitate the diagnosis in the latter group
lly realised that a new diagnosis is often brought
to explain clinical mysteries, and many such
have afterwards fallen into disrepute because
soon became too popular Bearing this in mind
osis of cervical myelopathy has never been made
aution The physical signs particularly in
III and IV have been verified by more than one

### *Treatment*

The best method of managing patients with cervical myelopathy has not yet been established and difficulties are increased by an ignorance of the course of the disease, especially in groups II and III

In group I conservative measures such as a collar combined with physiotherapy and active rehabilitation should be employed first Good results were observed in 6 patients, and the progression of the disease was halted in all of them. Assessment of results is difficult however because the natural course of the disease varies considerably and is characterised by periods of arrest The degree of recovery has never been great and full return of function seems unlikely; the importance of early diagnosis and treatment is thus evident. Extensive bed rest has not been used in these cases and it seems unlikely that it has any part in therapy It may even be contraindicated for in 2 cases (case 1 is one of them) the patient's condition deteriorated when he was immobilised Neck traction is also of limited application (Brain 1954b and c) Only 1 patient having failed to respond to medical management, was operated upon and in this case though little improvement has taken place it is hoped that the advance of the disease has been arrested Surgery seems to play a less important part than some would maintain (Ricard and Masson 1951 Müller 1951 Guillaume and Caron 1954 Semmes and Murphey 1954) and a study of the whole problem of therapy is being undertaken The problem is perhaps most difficult in the early stages of the disease (case 3) for our knowledge of these cases is limited Conservative handling with close observation and consideration of laminectomy should the disease continue to progress seems to be the most satisfactory approach

Group II patients received similar treatment to those with uncomplicated root syndromes Neck traction is not necessarily contraindicated. But the patient must be observed with care because of the evidence of myelopathy and should cord signs increase a collar should be used

In group III treatment directed at the cervical spondylosis is obviously not desirable The results of further study will determine future measures

The patients in group IV present individual problems but the methods of treatment are the same

Many interesting questions arise especially in groups III and IV Much more work is needed and, as Pallis et al (1954) have suggested the neurology of old age requires revision with cervical myelopathy in mind Such studies as that of Lassek (1944) on the extensor plantar response in health and in disease must be reconsidered, and further evaluation is needed of patients with non neurological disorders who have inexplicable involvement of the nervous system There are also some complicated neurological cases which might profitably be reviewed to ascertain whether cervical spondylosis is in any way responsible for their condition

## Summary

Spinal-cord compression due to cervical spondylosis (cervical myelopathy) is a common disorder

A series of 32 cases seen during fifteen months is divided into three groups according to the severity of the clinical picture A fourth group is made up of patients with other diseases neurological or non neurological who, in addition have cervical myelopathy

This condition may explain some of the spurious signs and hitherto inexplicable neurological features discovered in the healthy and the diseased state

I am grateful to the physicians of the department of
cine Postgraduate Medical School for allowing me to p
their cases, and to Dr Hugh Davies who kin
most of the myelography

*References overleaf*

# OSTEO-ARTHRITIS DEFORMANS OF THE LUSCHKA JOINTS

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*With illustrations on plate*

IT is currently fashionable to ascribe a significant proportion of cases of cervico brachial neuritis to a herniation or protrusion of the cervical intervertebral discs, in particular to an alleged lateral (or dorsilateral) protrusion of disc tissue into the intervertebral foramen (Frykholm 1951, Brain et al 1952, Brain 1954) The present paper directs attention to a more obvious and ubiquitous cause—namely, a deforming osteo arthritis of the joints of Luschka (neurocentral joints), a disease which constitutes, in our opinion, the commonest mechanical cause of cervical nerve-root irritation

Previous authors have described Luschka-joint osteo-arthritis and its sequelæ, without, however, gaining much notice or modifying a persistent preoccupation with disc lesions

Thus, Braun (1875) and Thoma (1931) recognised neuro central apophysitis as likely to compress the blood vessels of the cervical spinal nerves, with resultant œdema or congestion of the nerves, and Elliott (1926) knew that "spinal arthritis" could produce radicular symptoms by an osteophytic narrowing of the cervical intervertebral foramen. Gra described the characteristic radiological Luschka joint disease (his "arthrosis deformans bralis") and stressed the important relation of the apophysis to the spinal nerve Rathcke (1934) a (1937) denied the validity of Luschka's joints, but in the same situation "exostoses" which they be to differ from vertebral exostoses elsewhere Torgersen (1940) confirmed the distortion and the cervical intervertebral foramen by apophyseal and emphasised the likelihood of direct pressure phytes on the contained nerve and its vessels and the vertebral artery and nerve

Our own studies convince us that the Luschk tions are constant, normal, and necessary f the cervical spine that they are commonly th an osteo arthritis which always tends to intervertebral foramen, with or without inv its contents (figs 2b, 3b, and 4) and that the supposedly resulting from lateral herniation intervertebral disc is attributable rather to irritation, or compression of the cervical spin by an osteo arthritic Luschka joint

Our study is based upon the examination of changes in a series of 50 macerated cervical spin of known age and sex (see table), upon the dissection of a further 10 adult cervical sp particular reference to articular and disc ch upon the clinical and radiological examin unselected patients attending the surgical department of St Bartholomew's Hospital with toms or signs of cervico brachial neuritis. A of typical case-histories is given below

## Anatomy

### *The Luschka Joints*

The *Halbgelenke* of Luschka (1858) are bilater obliquely disposed paradiarthroses, situated axis and third vertebra and between each of ing cervical vertebræ By permitting the al movements of lateral flexion and rotation, neck its characteristic mobility The articular of each joint are formed by (1) the neurocentral (eminentia costarum, Luschka, processu Trolard) below and (2) the inferolateral vertebral body above The apophysis exhi an anterior non articular area (in contact with th and a posterior articular area Each apophysis, attached capsular ligament, forms the anter parietes of the cervical intervertebral foramen must restrain the disc from protrusion into the (fig 3c) The joint cavity (which is constant) medially by the periphery of the disc, later distinct capsular ligament

### *The Cervical Intervertebral Foramen*

This foramen is essentially a short canal ventromedially by the Luschka joint, dorsol the contiguous cervical articular pillars and zygapophyseal joint, and superiorly and infer relevant intervertebral (pedicular) notches ( 2a) At the medial extremity of the foramen and posterior nerve roots (the latter bearing unite to form the mixed spinal nerve, whic less in length, rapidly divides into ventral primary rami. The spinal nerve is nothing anterior and posterior nerve root fibres rearrangement into primary rami The arachnoid invests the respective nerve roo "root sleeves" of some writers) as far at medial extremity of the foramen the prote dura continues distally over the roots (th "root pouch") and the ganglion to become with the perineurium of the spinal nerve vertebral foramen (figs 1a, 2a, and 3a) is large its contained spinal nerve it is also occupi

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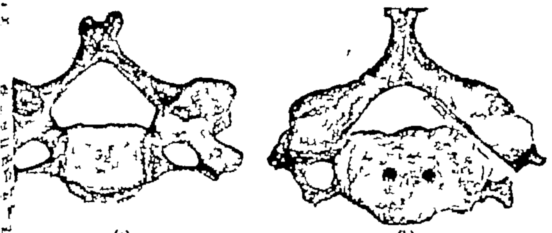
INCIDENCE OF LUSCHKA-JOINT OSTEO ARTHRITIS IN 50 MACERATED CERVICAL SPINES

| nd | Jt 3/4 |  | Jt 4/5 |  | Jt 5/6 |  | Jt. 6/7 |  | Age and sex | Jt 3/4 |  | Jt 4/5 |  | Jt 5/6 |  | Jt 6/7 |  |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|  | R | L | R | L | R | L | R | L |  | R | L | R | L | R | L | R | L |
|  | − | − | − | − | − | − | − | − | M 69 | − | (+) | − | − | − | (+) | − | − |
|  | − | − | − | − | − | − | − | − | M 59 | − | − | + | + | + | + | + | + |
|  | − | − | − | − | − | − | − | − | M 60 | − | + | − | − | − | − | − | − |
|  | − | − | − | − | − | − | − | − | M 60 | − | − | − | − | (+) | + | (+) | + |
|  | − | − | − | − | − | − | − | − | M 60 | − | − | (+) | − | + + | + | − | + |
|  | − | − | − | − | − | − | − | − | M 60 | + | + | − | − | − | − | − | − |
|  | − | − | − | − | − | − | − | − | M 61 | + | + | (+) | (+) | − | − | + | + |
|  | − | − | − | − | − | − | − | − | M 62 | (+) | (+) | − | − | + + | + + | + + | + |
|  | − | − | − | − | − | − | − | − | M 62 | + | − | + | + | + | + | + | + |
|  | − | − | − | − | − | − | − | − | M 63 | − | − | (+) | (+) | (+) | (+) | − | − |
|  | − | + | − | − | − | − | − | − | M 63 | (+) | (+) | − | − | − | − | − | − |
|  | − | − | − | − | − | − | − | − | M 64 | − | + | − | − | + + | + | + + | − |
|  | − | − | − | − | − | − | − | − | M 64 | − | + | − | + | − | − | + | + |
|  | − | − | − | − | − | − | − | − | M 65 | − | − | + + | + | + + | + + | − | + |
|  | − | − | − | − | − | − | − | − | F 66 | − | + | − | − | − | − | + | − |
|  | + | + | + | + | + + | + + | (+) | (+) | M 66 | + + | + + | + | − | − | + | − | − |
|  | − | − | − | − | − | − | − | − | M 66 | + | − | − | − | − | − | − | − |
|  | − | − | + | + | + | + | − | − | M 69 | + | − | + | − | + | + | + | − |
|  | − | − | + | + | − | − | − | − | M 70 | − | + | − | + + | − | + + | + | + |
|  | − | − | + | + | − | + | − | − | M 7 | − | − | + | + | + | − | − | − |
|  | + | + + | + | − | − | + | + | − | M 73 | + + | + + | + + | + + |  | + | + | + |
|  | − | − | − | − | − | − | − | − | M 75 | + | + | − | − | − | − | − | − |
|  | − | − | + | + | + | + | + | + + | M 77 | + | − | + | + | + |  | (+) | (+) |
|  | − | − | − | − | + | − | − | − | M 77 | − | + | − | − | + | + | − | − |
|  | − | − | + | + | + + | + | (+) | + | M 81 | + + | + + | + + | + + | + + | + | + | − |

stortion of neurocentral apophyses and of intervertebral canal. (+) = mild degree of distortion + + = severe degree of distortion

t arteries an abundance of veins and much soft uid extradural fat The cervical nerve is thus accommodated and is well protected against le *compression during movement* Its *position* the foramen remains constant save for a slight l shift during flexion But it lies in intimate and able contact with the Luschka joint (fig 3c), *ation of which is invariably dorsilateralwards*—i e e medial end of the intervertebral foramen Such ation and encroachment into the foramen produces iderable abnormal angulation of the nerve root causing irritation and even compression of the root fibres and their sheaths

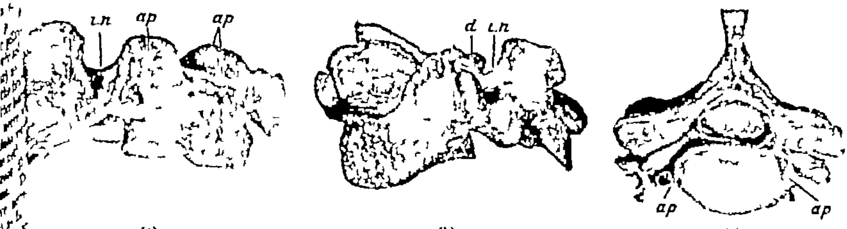

(a) (b)

(a) Normal cervical vertebra (cranial aspect) showing capacious intervertebral icular) notches; (b) cervical vertebra (cranial aspect) showing narrowing of vertebral notches by osteo-arthritis of the Luschka articulations.

## Pathology

The characteristic lesion is an 'osteo arthritic' deformity of the neurocentral joint with consequent bony encroachment upon the intervertebral foramen and a compression angulation of the contents of the foramen The articulating surfaces concerned are generally distorted (pitted and eburnated) enlarged and splayed laterally towards or into the medial end of the intervertebral canal (figs 1b 2b 3b and 4) These changes may be the only abnormality present throughout the entire cervical column as the majority of our specimens and cases show Very occasionally (in 0 8% of our cases) concomitant osteo arthritic change in the cervical zygapophyseal joints still further occludes the intervertebral foramen but it can be dismissed as a factor of any importance in distorting the foramen

*Osteophytic senile "lipping" of the caudal borders of* the cervical vertebral bodies may co-exist with Luschka joint arthritis for both are equally characteristic of the later decades of life but this is only a fortuitous asso-



(a) (b) (c)

(a) Normal cervical vertebra (right lateral aspect) showing wide intervertebral notch (*i.n.*) and height of neurocentral apophysis; (b) cervical vertebra (left lateral aspect) showing distortion (*d*) of Luschka-joint apophysis and consequent narrowing of inter- bral notch; (c) normal cervical vertebra (caudal aspect) with apophyses (*ap*) of subjacent vertebra in situ to show intimate relation ophyses to intervertebral canals and contents (dissected on left, undissected on right) and to intervertebral disc ciation, since neurocentral apophyseal osteo arthritis may occur in the absence of vertebral lipping, and the converse may also be true This lipping is more like an attempted ossification of the anterior common ligament, and we know no valid evidence that it is a cause of protrusion of the intervertebral disc

Senile shrinkage of the cervical intervertebral disc may be a cause of Luschka-joint arthritis In patients and cadavers of early middle life the disc often shows no detectable diminution in height (thickness) and radiography and dissection show that any abnormality present is confined to the neurocentral joints In later life, however, there is a varying degree of shrinkage of the disc, as part of the general vertebral changes of senile atrophy The precise cause of the osteo arthritis which deforms the neurocentral joints remains obscure, as does the cause of osteo arthritis elsewhere in the spinal column Shrinkage of the disc may be at least a predisposing or precipitating cause, for if the neurocentral arthritis results from a disturbance of the joint's normal mechanics, then shrinkage of the disc may help to produce arthritis by bringing a given neurocentral apophysis into abnormally extensive contact with the superjacent vertebral body

Nevertheless it is clear that there is no constant correlation between the degree of disc shrinkage and the distribution and severity of neurocentral osteo arthritis Thus, 5 of the 12 patients described in the accompanying case histories showed shrinkage in (usually) the lower neck, but in 2 only of these could any plausible connection be established between the shrinkage and the localisation and severity of the disease And, significantly, the adjacent zygapophyseal joints were normal

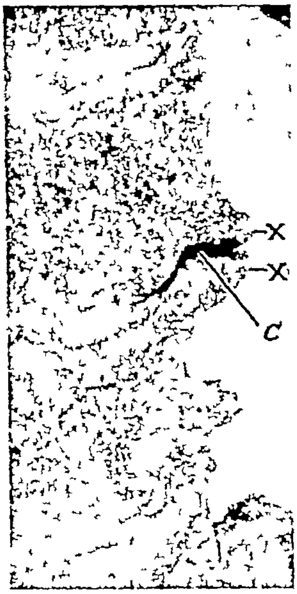


Fig 4—Frontal section through cervical spine, to show derangement of a Luschka articulation by osteophytes (C = joint cavity, XX = enlarged distorted joint surfaces)

### Radiology

In all our patients lateral oblique films of the cervical spine showed some encroachment upon the intervertebral foramina by osteophytes from the Luschka joints (fig 1b) Usually a number of foramina were narrowed, generally bilaterally, only once was a single foramen affected The precise degree of narrowing was not related directly to the severity of the disease, for symptoms result, not from compression by osteophytes, but from excessive angulation (and consequent irritation) of the spinal nerve by the osteophyte mass where the nerve enters the medial end of the intervertebral foramen This angulation and irritation of the cervical spinal nerves is comparable to that first recognised, though on a different mechanical basis, for the lumbar spinal nerves by O'Connell (1943)

Not every neck with radiological evidence of Luschka joint arthritis necessarily gives rise to symptoms On the other hand, in every patient in our series (they all had cervico brachial neuritis) radiological evidence was invariably present Radiology, therefore, can confirm suspected [illegible] lesions, but it gives no guide to the severity

Zygapophyseal osteo arthritis was also present in 1 instance This disease produces no symptoms; its occurrence merely emphasises the fact that, in the where the intervertebral foramen is very narrowing of the foramen does not, per se, symptoms A foramen may be considerably and yet there are no symptoms to produce there must be irritation of a spinal nerve by angulation over (behind) a distorted Luschka

In a third of our clinical cases the cervical disc found radiologically to have shrunk, as expected age, in the remainder the discs were depth The discs most often affected were 6/6 —that is, the discs situated where cervical is greatest

Anterior lipping of the cervical vertebral bodies ossification of the anterior common ligament, few cases, are unrelated phenomena due to age.

### Illustrative Cases

In these examples vascular lesions such as disease and vertebro costal anomalies (cervical reduced first rib) were excluded

Case 1—A woman of 64 had had three months' the radial border of the right arm, with paræsthesia 1st, 2nd, and 3rd digits pain was accentuated by cervical movement (rotation, lateral flexion) Sensibility diminished in the distribution of the median nerve right hand There was no muscle wasting, but weakness of the grip X-ray examination showed Luschka osteo arthritis was present in C5–7, and the diminution in height of disc 6/7

Case 2—A woman of 53 gave one month's history lateral cervical pain, radiating to the shoulder and clavicular region pain was persistent and accentuated ipsilateral cervical movement There was spasm of cervical muscles and consequent restriction of Cutaneous sensibility was diminished in the arm anterior primary rami of C3 and 4 No motor changes demonstrable Radiologically Luschka osteo-arthritis present in C3–6, and the disc space C6/7 was There was some ossification of the anterior common

Case 3—A woman of 49 had had several years the left index and middle fingers, with paræsthesia recently she had had pain in the left side of the neck tuated by ipsilateral cervical movement There disturbance of cutaneous sensibility The left was diminished, and the left thenar muscles were and weak Radiography showed marked Luschka arthritis in C3–7 The disc spaces were unchanged.

Case 4—A man of 42 gave a history of nine months starting in the neck and left shoulder and later along the radial border of the forearm pain was accentuated by ipsilateral cervical movement Cutaneous was diminished over the greater part of the extensor of the left forearm There was no muscle spasm or weakness in the neck or arm. Incipient Luschka arthritis was seen in C3–7 in X ray films The disc were unchanged

Case 5—A man of 50 had had one year's pain left shoulder and in the left supraclavicular region to the radial border of the upper limb and by ipsilateral cervical movement Recently pain in the cutaneous distribution of C2 and 3, and the paræsthesia of the left thumb and index finger triceps jerk was diminished. Muscle wasting and were absent Radiography showed Luschka in C4–7 The disc spaces were unchanged

Case 6—A woman of 62 had had right cervical six weeks, radiating to the shoulder and ipsilateral cervical movement She had spasm of the muscles on waking No motor or sensory changes demonstrable There was Luschka osteo arthritis The disc spaces were normal.

Case 7—A woman of 63 had had pain in the right triangle and shoulder for six weeks it was accentuated ipsilateral flexion and contralateral rotation There the neck or arm scaleni showed intermittent spasm. On X ray examina Luschka osteo arthritis was seen in C3–6 The disc s were diminished (from senile atrophy) below C1 here was much lipping of C3–7 and ossification of the or common ligament between C6 and 7

E 8 —A man of 49 had had several weeks pain radiating the lower neck over left shoulder with occasional severe bations. Residual pain was accentuated by ipsilateral al movement There were no other symptoms and no al signs. Luschka osteo-arthritis was present in C3–6 isc spaces were undiminished

E 9 —A woman of 58 gave a history of numbness ess, and pain in the right upper limb chiefly along the border of the forearm. Pain was worse at night ccentuated by contralateral cervical movement She aræsthesia and weakness of the right hand and loss of ion to pinprick in the distribution of the ulnar nerve in me hand but no cervical pain. The right triceps jerk minished Luschka osteo arthritis was visible in C4–7 o disc space 6/7 was diminished

E 10 —A woman of 51 had had ten years pain in the side of the neck radiating over the right shoulder and ing the radial border of the right forearm pain was ed by ipsilateral cervical movement She was unsuc ly treated by periodic manipulation at an osteopathic Recently pain had spread to the left side of the neck, ad not extended to the left upper limb She had hesia of the right hand The right triceps jerk was shed Luschka osteo-arthritis was seen in the radio in C4–6 and there was slight antero inferior lipping 7 The disc spaces were unchanged

E 11 —A man of 56 had had several weeks pins and in the left side of the neck to the point of the left or Luschka osteo-arthritis was visible in C3–7 and itant zygapophyseal osteo-arthritis of C3 further d narrowing of the intervertebral foramen. The disc were normal

E 12 —A woman of 45 gave a history of four years ver the right shoulder and supraclavicular region with it history of one month s pain along the radial border right forearm worse at night and on contralateral l movement She had occasional paræsthesia of the and. There were no physical signs. Radiographically a osteo arthritis was present in C3–6 The disc spaces nd 6/7 were diminished with pronounced antero lipping of C5–7 bodies

## Clinical Features

o arthritis of the Luschka joints is a common of insidious onset declaring itself most often in h and sixth decades of life (see table) but beginning frequently in the fourth As with osteo arthritis ere, it is progressive and an increasing number of ka joints become involved in the later decades and dividual distortion of each joint becomes more nced Trauma is not a cause and characteristically vical zygapophyseal joints are normal The clinical is a cervico brachial neuritis of high ' low ixed variety involving the roots of the cervical brachial plexus or of both The syndrome which ical of a mechanical irritation of the cervical roots includes in order of importance pain hesia diminished sensation to pinprick diminished muscle weakness and rarely muscle wasting

stant pain is always a symptom and is the usual of relief being sought It most commonly radiates the radial border of the arm and forearm (in tribution of C5 and 6) and it is very often associated similar kind of pain in the neck (distribution of 4) Characteristically such pain is intensified e ipsilateral (sometimes contralateral) cervical ent of lateral flexion and rotation but is unaffected flexion pure extension or rotation at the axial articulations It is often therefore worse king because of unconscious cervical movements sleep The onset of symptoms may be sudden dual and in either case subject to remissions for periods of up to six months or longer

Paræsthesia is also present in about 75% of patients and usually affects the hand (thumb index and middle fingers)

Physical signs are less obtrusive Some one third of patients have diminished sensation to pinprick or a diminished triceps reflex less than one third show weakness of the hand muscles or thenar wasting Spasm of the scaleni and deep cervical muscles may be present

Diagnosis depends on (1) the nature and distribution of the pain and/or paræsthesia (2) intensification of pain on cervical movement (generally ipsilateral) (3) the mode of onset and remissions (4) the age of the patient and (5) confirmation by lateral oblique radiographs of the neck

## Treatment

Obviously neurocentral apophysectomy of the affected joints is the only means of permanent cure but how practicable such an operation may prove when a number of Luschka joints are involved we are not competent to say Palliative therapy apart from analgesics includes long courses of short wave diathermy (which may induce a remission) and immobilisation of the cervical spine by for example a plastic or plaster collar splint (which may afford relief during acute phases) In our opinion neck traction or manipulation is valueless and is likely to aggravate symptoms

## Summary

Osteo arthritis of the cervical neurocentral (Luschka) joints is described from anatomical and clinical material with special reference to its ubiquity and age incidence

The disease is shown to be responsible for narrowing of the intervertebral foramina with consequent angulation and mechanical irritation of the cervical spinal nerve roots

We tender our appreciation to Mr D F Ellison Nash and to Mr Alan H Hunt for permission to examine patients under their care at St Bartholomew's Hospital and to Dr R A Kemp Harper for radiographic facilities in the hospital The photographs are the work of Mr A E Westwood

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# THE ONYCHODERMAL BAND IN HEALTH AND DISEASE

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*With illustrations on plate*

EACH nail bed has two clearly differentiated zones— the half moon and the larger distal pink area On close examination a third zone can often be identified in normal people it forms a barely perceptible pale narrow band, and runs transversely across the distal portion of the nail bed immediately proximal to the free edge of the nail I call it the onychodermal band and the rest of the pink area I call the main pink zone

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The main pink zone may become whitened (especially in hepatic cirrhosis), giving the appearance known as "white nails" (Terry 1954a), and the half-moons may become reddened, especially in chronic heart failure in older persons (Terry 1954b) Since it seemed likely that the onychodermal bands too would be affected in some disorders, special attention was given to them in all further observations upon the nails, and changes were in fact encountered, although much less often than in the other two zones The purpose of this paper is to describe the appearance of normal and abnormal onychodermal bands, and to discuss their significance

### The Onychodermal Band in Health

In the finger nails the onychodermal band is usually 0 5–1 5 mm wide, but there are many exceptions Commonly the band is narrower and less apparent in the thumb-nail (unlike the half-moons, which are more prominent in the thumbs) The band is paler than the main pink zone, and has a slightly amber tinge and a faintly translucent quality, in Negroes, it sometimes has a trace of brown pigmentation Often a fine transverse white line may be made out at the junction of the band and the main pink zone These appearances are difficult or impossible to see unless the fingers are pointing directly at a good source of light, preferably the sun

### The Onychodermal Band in Disease

Of 2500 patients in general medical and surgical wards, 9 had onychodermal bands which were much more prominent than usual, the prominence resulting from an exaggeration of the characteristics of a normal band These abnormal bands were readily visible from a distance of at least four feet Though their whiteness did not possess the ground glass quality of the half-moons, it did preserve both the suggestion of pale amber and the translucent quality In 1 patient the bands were ivory-coloured, this patient had generalised keratosis Squeezing blood into the finger tip did not diminish the onychodermal band, indeed the contrast between the band and the congested main pink zone was accentuated

These 9 patients consisted of 5 with hepatic cirrhosis, 1 with thyrotoxicosis (fig 1), 1 with pulmonary eosinophilia, 1 with malnutrition, and 1 with keratosis

In 3 of the patients with hepatic cirrhosis there were also "white nails" This was interesting, since the juxtaposition of the abnormal onychodermal bands and the opaque main pink zones permitted the two conditions to be readily compared The opacity of the main pink zones stopped short of the abnormal onychodermal bands, and in each nail there was a narrow pink line of normal nail-bed intervening between the onychodermal band and the "white nail" (fig 2) The ground-glass opacity of the "white nails" had none of the faintly pigmented and translucent quality of the opaque bands, and this difference is apparent in monochromatic as well as polychromatic reproductions

In a recent description of "white nails" (Terry 1954a), I remarked that the whiteness usually terminated 1 0–2 0 mm. short of the distal edge of the nail bed, and I termed this narrow unaffected area the "distal pink zone" It is now apparent from further studies on "white nails" that the distal pink zone is formed by the onychodermal band

Changes in the onychodermal bands were also noticed in 2 patients with paronychia At the onset of the infection the bands were not remarkable Following resolution of the infection, there was desquamation of the skin of the terminal phalanx, and when this reached the distal portion of the nail, the bands became increasingly opaque and finally assumed a dense white colour without either pigmentation or translucency (fig 3)

onychodermal bands have been seen in both

neral skin disorders

### Anatomy

Examination of the under surface of a dry is instructive In the region of the main pink nail has a rough, unpolished appearance, whil areas corresponding to the half moon and the dermal band, the nail is smooth and shiny W rough area joins the smooth areas, small ragged may often be seen The superficial layer of the is apparently attached firmly to the nail only in th of the main pink zone Hence, when the nail is the superficial layer of the nail bed is also giving it a rough appearance, whereas in the of the onychodermal band (and of the half mo superficial layer remains attached to the nail bed

This loose attachment of the onychodermal demonstrated in everyday life by people who us nail-files to clean their nails if they are clea may separate the nail from the onychodermal Another common cause of separation of the nail band is nail-biting, which causes the onych bands to disappear Separation of this type is in contrast with the painful separation of the the main pink zone This can be demonstrated dramatically with a needle the point of the need be inserted between the nail and the onychoderm without discomfort, but, immediately the prox of the band is crossed and the main pink zone exquisite pain is experienced

The onychodermal band offers some slight to pathological processes in the main pink zone the main pink zone small hæmatomata and have been observed to have straight distal bord they were being temporarily obstructed by the dermal band As the abscess grows, it spreads *under* the onychodermal band On the other small hæmatoma grows out with the finger nail lie *superficial* to the onychodermal band, and scraped away from the under surface of the fre the nail The reason for the different behaviour abscesses and small hæmatomata is not clear

Fig 2 provides further proof of the difference the onychodermal band and the main pink zone centre of one nail there were several longitudinal the result of an injury many years previously this strip of ridges, the opacity of the "white na replaced by the normal pinkness of the main pin but the abnormal opaque onychodermal band unaltered by the ridges

The onychodermal band apparently has a blood-supply from the rest of the nail bed If th of the finger is pressed gently, there is blanching band and also of a small area of the nail bed to the band If this is repeated several times, th flushes Pressure on the centre of the dorsum of th on the other hand, causes blanching of the ma zone but not of the onychodermal band No studies have been made

### Discussion

There seem to be many reasons for thinking onychodermal band is related more to the adjac than to the nail-bed It appears to have a different supply and possibly a different blood suppl unaffected by a fault in the nail which affects th the nail bed, it is often pigmented in Negroes, involved in various local and general skin There is a thickened area of skin under the fre the nail known to dermatologists as the hypo it seems likely that the onychodermal band is a tional zone between the nail-bed and the hypon

The cases of opaque or abnormal onychoderm observed so far are too few in number to serious evaluation of their significance Since the have been observed in disorders known to be as

docrine disorders, and since well-developed bands
less marked than any in the abnormal group)
een seen in a few healthy subjects, one is tempted
gest that opaque onychodermal bands may be of
ne origin, except where the ætiology is clearly
ological However the purpose of this paper is
lly to record the characteristics of abnormal
dermal bands, in the belief that they are physical
hich should not be ignored.

## Summary

nt narrow band, the onychodermal band,' may
ntly be detected running transversely across the
portion of the nail bed in normal people
ertain diseases, a whitish opacity develops in the
odermal bands 9 examples of this condition have
bserved 5 of these were patients with hepatic
is
city of the onychodermal band constitutes a
al sign which may have clinical importance.

indebted to Miss Betty Gould and Mr N K. Harrison
photographic department St Bartholomew s Hospital
illustrations

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# A BARBITURATE ANTAGONIST

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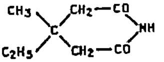
E months ago Shaw et al (1954) reported the
very of a barbiturate antagonist β,β methyl
glutarimide (designated NP 13):



ts mice, and rabbits NP 13 (15 mg per kg body
ht) antagonised pentobarbitone thiopentone and
tone anæsthesia, reducing the sleeping time by
and doubling the barbiturate-depressed respiration
In unanæsthetised animals NP 13 produced
ulations and/or generalised convulsions: with
of 30 mg per kg fatal convulsions occurred in
animals The intravenous injection of a barbiturate
ppropriate dose before or after the injection of
3 prevented or abolished these convulsions. During
barbitone anæsthesia in dogs NP 13 (15 mg per
restored the electro-encephalographic pattern to
al while overdose produced spikes

30 cases in which suicide had been attempted by
g barbiturates Shaw et al (1955) significantly
ened the period of coma using a mixture of NP 13
-4-diamino 5 phenylthiazole a morphine antagonist
is slightly antagonistic to barbiturates

## Observations

ofessor Shaw kindly let me have supplies of these
substances for tests during clinical anæsthesia and
e assessed their value in three types of case

e *first group* consists of fifty seven psychiatric cases
hich the patient was prepared for electrical shock
py (E C T) with thiopentone 0 5 g atropine gr $^1/_{66}$
*d* tubocurarine 30 mg The shock having been
and the attenuated clonic convulsions having
ded the subject was decurarised with neostigmine
hen given 50 mg of NP 13 and 15 mg of thiazole
venously through the same needle After the third
thiazole was omitted and the remaining 54 cases had only NP 13 In all cases, thiopentone anæsthesia was rapidly terminated, without fasciculations or convulsions The palpebral reflex was active within 30–60 seconds The patients pursed their lips and bit on their airway within 60–90 seconds. They ejected their airway in about 2 minutes and talked in an inebriated fashion within 3–4 minutes Within about 4 minutes of the injection of NP 13 the patient's state coincides with that observed 4 minutes after the completion of unprotected E C T, and it can be concluded that thiopentone anæsthesia is now completely abolished The response of the next group of subjects strengthens this conclusion

The *second group* consists of six subjects anæsthetised with thiopentone 0 5 g and atropine gr $^1/_{66}$ for orthopædic manipulations of the neck, spine and hips Here thiopentone anæsthesia is uncomplicated by the action of additional central depressants such as E C.T surgical shock, and/or surgical trauma The manipulations finished, these subjects were given 50 mg of NP 13 intravenously The palpebral reflex returned at once and they pursed their lips and ejected their airway Four of these subjects talked on the theatre table and the remaining two talked in the lift on the way back to bed

In these two groups it was noted that after the recovery produced by NP 13 the subject often lapsed into sleep again But this was natural sleep for external stimulus such as squeezing the wrist resulted in instant awakening with the startled response normally produced in a subject abruptly roused from natural sleep

The *third group* consists of ten surgical cases premedicated with hyoscine hydrobromide gr $^1/_{150}$ and Omnopon gr $^1/_3$ and anæsthetised with thiopentone 0·5 g and cyclopropane with appropriate *d* tubocurarine In these subjects surgical interference lasted from 10 to 45 minutes In two urethral dilatations lasting 10 minutes and in a cystoscopy for retrograde pyelography lasting 15 minutes recovery after 50 mg of NP 13 was rapid: the patients talked on the theatre table or in the lift on their way back to bed Six subjects for cystoscopy and fulguration of bladder papilloma lasting from 20 to 40 minutes who received 50 mg of NP 13 ejected their airway before leaving the theatre and talked within 3–7 minutes This delay in recovery compared with the second group can be attributed to the duration of cyclopropane anæsthesia After the same anæsthetic had been given for 40 minutes to a shocked patient with post prostatectomy clot retention the intravenous injection of 50 mg of NP 13 produced no observable response This can be attributed to the depressant action of cyclopropane anæsthesia and/or surgical shock

## Comments

Shaw states that NP 13 is quite innocuous and, using doses of 50 mg I have seen neither fasciculations nor any other side actions When the results in this series of seventy three cases are considered with Shaw s results in the treatment of barbiturate coma we may conclude that NP 13 is a barbiturate antagonist of real clinical worth To omit to use it in the treatment of barbiturate poisoning is to run the risk of the bronchopneumonia that is so often fatal in such cases Its use after surgical anæsthesia can be valuable but is more limited because the patient may be under the influence of central depressants other than barbiturates. In the hands of the biochemist it should prove a useful tool in investigating the nature of the affected biophase during narcosis

I wish to thank Prof F H Shaw for data and material and Dr N Cass for help and advice in carrying out the trial.

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# RECURRENT MOLLUSCUM SEBACEUM

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Though molluscum sebaceum or molluscum pseudocarcinomatosum (*Lancet* 1953) is now recognised by most British dermatologists as an entity and a benign tumour, its ætiology remains obscure Cases have been published in which the growth disappeared spontaneously (Rook and Whimster 1950, Gordon 1950, Beare 1953, Halnan 1953), but I have not been able to find any published report of a molluscum sebaceum which, having been observed to disappear spontaneously, grew again on the same site, nor any reference to occasional rapid and very alarming increase in size of the tumour after surgical interference These two features may be of value in any discussion on the ætiology of molluscum sebaceum and certainly will have to be explained by any hypothesis put forward to explain the causation The following case-reports may therefore be of interest

## Case-reports

**Case 1** —A woman, aged 62, attended the skin department of the Royal Victoria Hospital, Belfast, on April 1, 1953, with a typical molluscum sebaceum about 1 cm in diameter on the back of her left hand (fig 1*a*) The lesion had been present for six weeks The patient had no complaint other than that occasionally this nodule was painful when injured It was decide to leave this tumour untreated, and photographs showing its spontaneous disappearance were taken The clinical diagnosis was so obvious that a biopsy was not regarded as essential The patient was most coöperative and attended the department regularly

*Progress* —On April 15, 1953 (eighth week), there was very little change, except that the central keratin plug was a little larger (fig 1*b*) On May 27, 1953 (fourteenth week), the keratin plug was much larger and lifted off readily, and the peripheral part of the lesion showed early resolution (fig 1*c*) On June 30, 1953 (nineteenth week), the tumour was still (fig 1*d*) On Sept 3, 1953 (twenty-eighth week) it had completely disappeared but had left a superficial scar (fig 1*e*)

*Recurrence* —At this stage it was thought that no trouble need be expected, but on Sept 30, 1953, a papule $^{1}/_{8}$ in in diameter was noted at the proximal of the scarred area, and on Oct 21, 1953, this pap become slightly larger and was by now another molluscum sebaceum (fig 1*f*) It was considered to leave this alone, and the lesion was removed surgical excision, thereby supplying a good biopsy Histological examination confirmed the clinical of molluscum sebaceum and showed large amou formed keratin and pseudo epitheliomatous (fig 2)

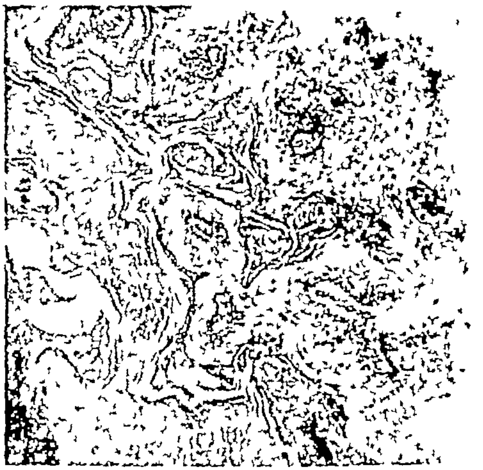

Fig 2—Biopsy specimen of recurrent molluscum sebaceum showing keratin and pseudo-epitheliomatous hyperplasia

**Case 2** —A man, aged 69, attended the skin the Royal Victoria Hospital, Jan 27, 1954, with a typical sebaceum of two months' duration cheek (fig 3*a*) This was removed planing off the top of the tumour scalpel and controlling hæmorrhage cautery

*Recurrence* —On Feb 16 a lesion as large as the original one was present same site This was at first left alone, March 2 it was larger than the orig on March 16 was relatively enormous, being 3 cm in diameter The ly glands were not enlarged However, clinical point of view a diagnosis of m sebaceum seemed correct, and the his appearance of the original fragment r on Jan. 27 was characteristic of mo sebaceum

*Treatment* —The recurring lesion treated with X rays 1500r, 90 kV, (inherent filtration 0 5 mm alumin March 16 The lesion was a little sm April 2, and the central keratin plug on April 7 Thenceforward rapid r took place, and by May 26 no abn was apparent other than some sl scarring (fig 3*c*) The patient remain

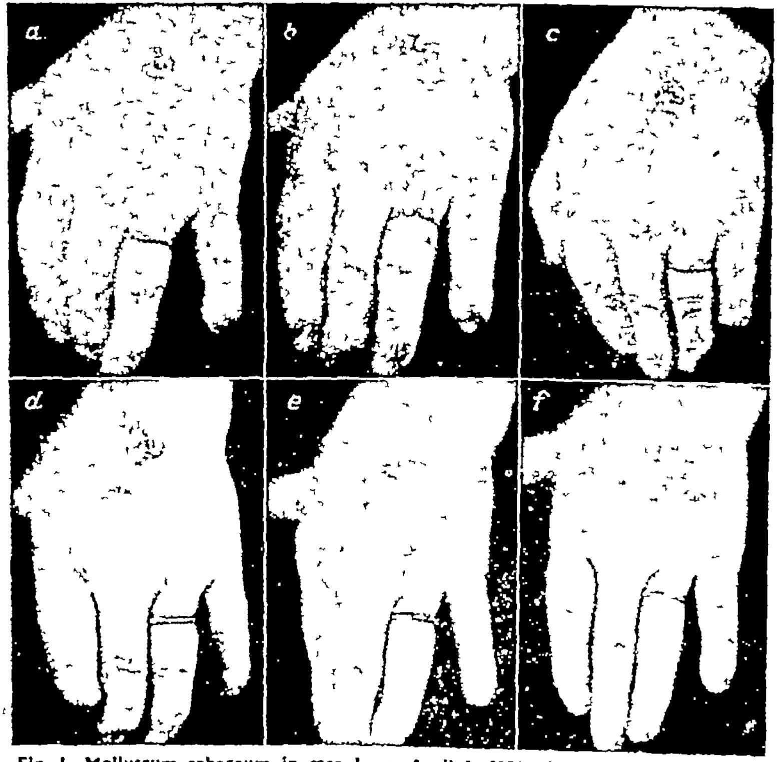

Fig 1—Molluscum sebaceum in case 1 *a* April 1, 1953 *b* April 15 *c* May 27 *d* July 30 *e*, Sept. 3 *f* Oct. 21

## DISCUSSION

Since January, 1940, 122 of tumours have been studied, includ 76 seen up to February, 1952, and reported (Beare 1953) The treatment has been planing off the t getting a biopsy specimen, follow application of the cautery This trea seems to be satisfactory Apart

, in which an alarming state of affairs developed
urgical intervention of this type, and case 1, which
ot treated at all there have been 3 other recurrences
present series (1) a lesion, as big as the original,
ed eight weeks after treatment and was removed
e same method this time satisfactorily (2) a
ence was noted three months after curettage
y, and X rays 1200r 00 kV 5 mA (inherent
on 0 5 mm. aluminium) and was satisfactorily
ed by curettage and (3) a small nodule recurred
nth after simple planing and cautery and was
ctorily removed by the same method

ncy (1954) showed that these tumours can be
d with a relatively low dose of X rays—1500–
The important point now firmly established,
t the lesion usually responds to simple therapy,
hat the therapeutic techniques used for the treat-
of malignant skin lesions, whether surgical or radio
are quite unnecessary and indeed undesirable
inted out in *The Lancet* (1954) It is no less
lling to save a patient with a benign lesion from the
nforts anxieties and dangers of treatment for

rapid increase in size of the lesion in case 2 after
al interference was unique in the present series but
bled the state of affairs which occasionally follows
nge of warts, especially plantar warts, when after
al removal of a small lesion an enormous verrucous

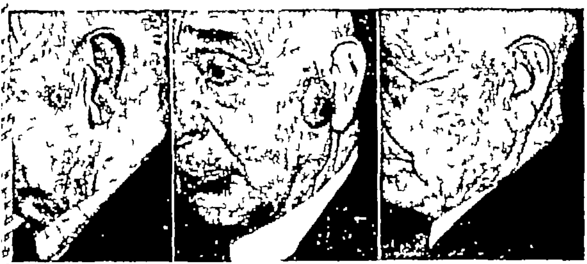
a b c

Fig 3—Molluscum sebaceum in case 2: a Jan. 27 1954; b March 16; c, May 26.

levelops. Most of those who have treated many
r warts have probably seen this unfortunate and
rassing complication Occasionally the mass which
s is too large to allow of a further attempt at
al removal Since plantar warts are a virus
on it is tempting to regard molluscum sebaceum
a virus infection Case 1 however would be more
lt to explain on a basis of virus infection and
ts to reproduce the condition experimentally by
ng crude filtrates of the tumour have so far failed
1953)

### Summary

molluscum sebaceum disappeared spontaneously
as followed almost immediately by a recurrence
same site

ther molluscum sebaceum grew to an enormous
ter it had been partly removed surgically

D H R McLaffey was responsible for figs. 1–3*a*

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# TREATMENT OF LEAD POISONING
## WITH CALCIUM DISODIUM VERSENATE

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The use of the calcium complex of ethylenediamine tetra acetic acid (calcium disodium versenate) in the treatment of lead poisoning was first reported in 1952 (Bessman et al ) Its efficacy has been confirmed in several subsequent reports (Belknap 1952 Rubin et al 1953 Karpinski et al 1953 Bessman et al 1954, Byers and Maloof 1954, Hardy et al 1954) all relating to intravenous therapy Sidbury et al (1953) and Bradley and Powell (1954) have recently used an oral preparation with benefit in cases of chronic poisoning All the reports are from the United States.

### Case-report

A boy aged 2½ was admitted to hospital on Sept 6 1954 He had been chewing and sucking objects all his life and for 6 months had been gnawing lead-covered telephone wires on the balcony of his home 3 weeks before admission he began to have morning vomiting and to be unwontedly irritable 2 days before admission he became listless vomited through the day, and complained of abdominal pain. The drowsiness increased and he apparently began to have some difficulty with micturition but otherwise his symptoms remained unchanged until his admission.

*Examination*

On admission the child was pale ill drowsy and lay curled up on his side resenting any interference There were no other abnormal clinical signs.

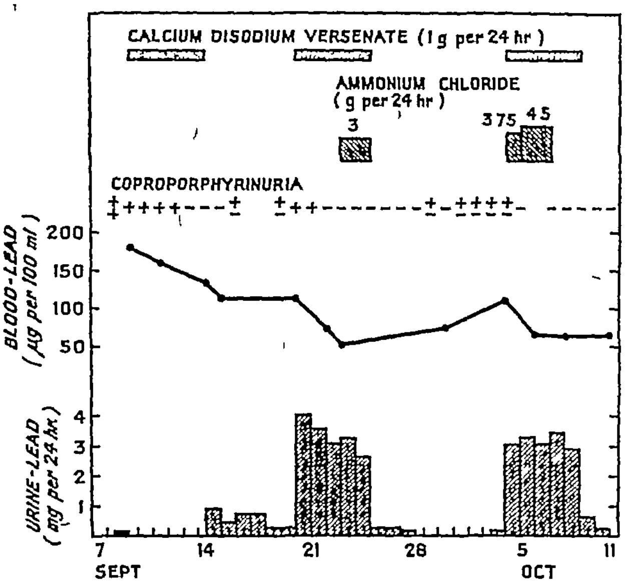
2 days after admission immediately before the first infusion of calcium disodium versenate a generalised convulsion took place which lasted an hour

*Investigations*

In addition to the investigations recorded in the accompanying table and figure the leucocyte-count was 15 000 per c.mm (3 late normoblasts per 100 leucocytes) the serum bilirubin 0·8 mg per 100 ml., and Ehrlich's urinary urobilinogen test was positive at 1 in 20 dilution The cerebrospinal fluid (C.S.F ) contained 3 leucocytes per c.mm Radiographs of the long bones showed dense bands at the metaphyses consistent with heavy metal poisoning An electro-encephalogram showed activity at 8 cycles per sec and, during sleep irregular activity of moderately high amplitude at 3–5 cycles per sec Lead poisoning was diag

BLOOD AND CEREBROSPINAL-FLUID INVESTIGATIONS

| Date | Hæmoglobin (g per 100 ml ) | Reticulocytes (per 100 red cells) | Stippled cells (per 300 red cells) | Blood urea (mg. per 100 ml ) | C.S.F protein (mg per 100 ml ) |
|---|---|---|---|---|---|
| Sept. 7 | 8 9 | 6 | 6 | 51 | 100 |
| 10 | 9 6 | | | | |
| 14 | 8 1 | | <1 | | |
| 17 | 9 6 | 4 | 3 | 43 | 60 |
| 21 | 10 4 | 1 | 3 | 41 | |
| 24 | 10 4 | | <1 | | |
| 28 | 11 1 | 1 | <1 | 46 | 10 |
| Oct 5 | 13 3 | | 0 | 33 | |
| 11 | 11 0 | 1 | | 37 | |
| ,, 21 | 12 6 | 1 | <1 | 46 | |



**Effect of calcium disodium versenate and ammonium chloride on blood-lead levels and on urinary lead and coproporphyrin excretion**

nosed but treatment was withheld until a 24 hour urine sample had been collected for estimation of lead (see figure)

*Treatment*

Calcium disodium versenate was given intravenously at 12 hourly intervals (0 5 g in 200 ml of 0 18% sodium chloride in 4 3% dextrose), each infusion lasting some 2 hours Three 5 day courses of versenate were given, with intervening rest periods of 6 and 9 days

*Progress*

There were no further convulsions or vomiting after the first infusion of versenate The volume of urine increased rapidly from 194 ml to 1130 ml per 24 hours The patient's mental state improved steadily, and after 3 days he was bright and alert, he subsequently showed no further clinical evidence of lead poisoning

The lead levels in blood and urine, together with other serial investigations, are shown in the figure and table Except for a few samples obtained during or immediately after a course of versenate, his urine regularly gave a green reduction of Benedict's solution, albumin and casts were not found On Sept 15, liver function tests showed total protein 6 6 g per 100 ml (albumin 5 3 g, globulin 1 3 g), thymol turbidity 1 unit, alkaline phosphatase 12 6 King Armstrong units On Oct 1, fasting blood sugar was 100 mg per 100 ml On Oct 4, radiographs showed no change in the metaphyseal bands An electrocardiogram on Oct 14 was normal

He was discharged from hospital on Oct 17 When seen again on Oct 21, he was clinically well and his mental state seemed normal His urine continued to reduce Benedict's solution, and the coproporphyrin test was positive, the blood lead had risen to 85 µg per 100 ml His leucocyte count was 10,000 per c mm and platelets 150,000 per c mm, prothrombin time was 80% normal, bleeding time (Duke) 3 minutes, and clotting time (Lee and White) 5 minutes, serum calcium was 10 6 mg per 100 ml, and serum phosphorus 4 1 mg per 100 ml

## Methods

Urine was collected through a length of Paul's tubing strapped to the penis and leading to a Winchester flask previously treated with lead free nitric acid

*Coproporphyrin*

Urinary coproporphyrin was tested for by taking 5 ml of fresh urine in a test tube and adding 2–3 drops hydrogen peroxide, 5 drops glacial acetic acid, and 1–2 ml ether, after 10 minutes the other layer was inspected under a Wood's lamp for the characteristic reddish pink fluorescence

*Lead*

Determinations of the lead content of 5 ml blood and 20–50 ml urine were carried out as recommended by the Lead Panel (1954) "Wet ash" digestion was followed by extraction of dithizonate without using dithiocarbamate The the lead complex was measured on the Hilger ter, using the green filter (no 604, 520 mµ) This

technique, which varies only in detail from that Karpinski et al (1953), determines the total lead, combination with versenate and free In the first treatment the lead in the urine samples was unfor estimated by a method in which the lead is separated urine by co precipitation with calcium oxalate (Bl Allcroft 1950) before wet ashing At normal pH versenate did not co precipitate, and therefore only lead was determined (it was, however, observed th urine was strongly acidified—e g, with 10 ml. hydrochloric acid per litre—the lead versenate dissociated and all the lead was co precipitated calcium oxalate) After the first period of versenate both the free and total lead in the urine were de

For 2 to 3 days after stopping versenate, the remained at a higher level than the free lead, which that the excretion of lead-versenate complex contin that period this agrees with the observations of H (1954) During the second period of treatment the which in the preceding rest period had not fallen bel per day, diminished to 0 05 mg per day, although lead had risen at this time to between 3 and 4 mg.

## Discussion

Calcium disodium versenate is the calcium of ethylenediamine tetra-acetic acid (E D T A) is a chelating agent—i e, a substance capable of multivalent metallic ions so as to cause their removal from solution The stability of comp formed varies with the metal concerned, and forming a stronger complex can replace one weaker complex Thus lead displaces calcium calcium disodium complex, which for this reason in the treatment of lead poisoning The calcium must be used because E D T A alone would comb calcium in the plasma so rapidly as to cause hypo tetany and death (Popovici et al 1950) Exp on animals (Bauer et al 1952) have shown that disodium versenate causes no serious rea patient of Belknap's (1952) showed transient marrow depression, Bradley (1954) described changes in the electrocardiogram, and one of (1953) patients had abdominal pain and diarr high oral dosage, but no other definite toxic eff been reported in man

*Dosage*

Dosage has been somewhat empirical, but the mendations of Foreman et al (1953), based on animals, are as follows the drug should be give venously, and no faster than 0 5 g per 30 lb body per hour, the daily dose should not exceed 1 g p body-weight nor the weekly dose 5 g per 30 lb weight, and courses should be limited to 7 5 30 lb body weight given over 10 days, with 7- periods between courses Maison (1953) suggests drug should not be injected in a concentration than 3% Bessman et al (1954) give 0 5 g of 8 hourly for 5 days with 3 day rest periods. It is that such doses are unnecessarily large Su of calcium disodium versenate binds 1 mM 1 g (the recommended daily dose for a child could bind 553 mg of lead The maximum urinary lead excretion is, however, in all report that of Hardy et al [1954], which concerns adult 4 mg, this is likely to represent almost the versenate excretion, since it has been shown up to 99% of an intravenous dose of E D T A able from the urine (Foreman et al 1953) Cle a minute proportion of the lead-binding capacity administered calcium disodium versenate is util the fact that versenate has to compete for lead binding agents, such as the sulphydryl groups of (Bessman et al 1954), does not entirely rob this of its validity Moreover, figures quoted in other relating to patients who were given various versenate do not suggest that either blood- urinary excretions were increased by higher do *onse*

ur patient responded to treatment in much the same as the other reported cases Vomiting and convul ceased from the time that versenate was started the child rapidly became less irritable and more alert gradual disappearance of coproporphyrin from his , and of stippled cells from the blood the rise in oglobin, and the fall in blood urea and in o s.r in are recorded in the accompanying table and e Urobilinogen was present only in the first sample ine *glycosuria has persisted up to the most recent* Although as already mentioned lead estimations ig the first course of versenate were made by a od which does not assay lead complexed with A., the excretion figures for the second and third es *show clearly that the urinary output of lead* greatly increased by giving versenate Probably epresents an increase in total lead output, since the mum fæcal excretion observed by Aub et al (1925) in nts with lead poisoning was only 1 86 mg over a period, even if excretion by this route were letely suppressed during versenate therapy it would early cancel out the increase in urinary excretion

figures for blood lead levels show a steady fall unlike given in previous reports, which often showed a striking uring versenate therapy This may be related to the noted in experiments on animals that 60–90% of an enous dose of versenate is excreted within 6 hours man et al 1953) Blood samples were (with one excep- obtained a minimum of 9 hours after each versenate on If the previous workers obtained their samples during rtly after an infusion their results might well be differ but none of the published reports gives the information s point.

ere is ample evidence that calcium disodium nate effectively relieves the symptoms of acute poisoning moreover comparison of the amount of eliminated during treatment with the fall in blood levels suggests that stored lead must be removed nly from the blood but also from the tissues Much r quantities remain in the skeleton and elsewhere even after versenate treatment mobilisation may place and acute poisoning recur (e.g , in the course of ection or from other metabolic stress) It therefore d logical to try to increase the excretion of lead g versenate treatment by any available means as shown in the figure ammonium chloride was nistered on two occasions No effect was observed inary lead excretion ; this may have been because ate acidosis was not obtained—the blood pH fell o 7 38 and the plasma bicarbonate to 23 2 m eq tre (Oct 6)—or because the patient was not on a alcium diet (Aub 1935) or because ammonium de was not given for long enough The possibility ch controlled elimination of lead warrants further loration

### Summary

treatment with calcium disodium versenate of lead poisoning in a child of 2½ is described No effects from the versenate were observed Problems sage and the interpretation of changes in blood rinary lead content are discussed

ministration of ammonium chloride during versenate nent did not increase the urinary excretion of lead

work was undertaken at the suggestion of Dr R rood The calcium disodium versenate was supplied by Laboratories, Loughborough

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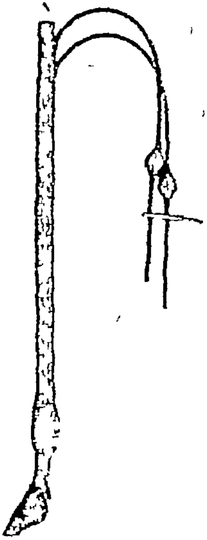
# New Inventions

## A NEW RIGHT ENDOBRONCHIAL TUBE

WE have designed an endobronchial tube for right-lung anæsthesia. This instrument permits ventilation of *all* the lobes of the right lung and facilitates transection and closure of the left main bronchus or of the tracheal wall

The tube (see figure) is made of rubber and has a cross section similar to a size 8 "streamline" Magill tube. The lower 4 cm is angulated *approximately 20* On this angulated portion of the tube is a slot 2 cm. long and 2 mm. wide. An inflatable cuff is attached to the margins of this aperture and surrounds the remainder of this portion of the tube A stiff rubber hook, similar to that on a Carlens tube,[1] projects from the angle of the tube opposite and 1 cm. above the slot. A second inflatable cuff, similar to that on a standard endotracheal tube, has its lower margin 2 cm. above the hook. The inflating tube of the lower cuff runs in the wall of the main tube, and that of the intratracheal cuff runs on the surface of the main tube



The tube is passed through the larynx under direct vision and advanced blindly down the trachea until the hook is felt to impinge on the carina The angled end of the tube will now lie in the right main bronchus. Inflation of the intratracheal cuff will help to stabilise the instrument and hold it in position When the lower cuff is inflated it will push the slot over the right upper lobe bronchial orifice and occlude the lumen of the right main bronchus. Now closed ventilation of the whole of the right lung *may be maintained When the left chest has been* opened, the intratracheal cuff can be temporarily deflated to allow the left lung to collapse to the extent required *After closure of the left bronchial stump both cuffs may* be deflated and while aspiration is performed through the tube the latter is withdrawn into the trachea The upper cuff is now reinflated to allow the adequacy of the bronchial closure to be tested

Rarely the right upper-lobe bronchus arises from the trachea In this case the tube cannot be used Therefore all patients should be bronchoscoped to determine the nature of the bronchial anatomy

The Gordon-Green Endobronchial Tube is obtainable from Messrs. A Charles King 27 Devonshire Street W 1

WALLY GORDON
F.R.C.S. F.R.C.S.E.

St George's Hospital
London

RONALD A GREEN
M.D Camb F.F.A.R.C.S.

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# Reviews of Books

## Into General Practice

*A Guide for the Beginner and Others* J G THWAITES, M B London Heinemann Medical Books 1954 Pp 223 12*s* 6*d*

THE aspirant to general practice could fill a bedside shelf with guide-books, some of which tend to duplicate each other, but Dr Thwaites in this non-clinical guide-book has made a distinctive and valuable contribution to the subject He aims at telling the reader what general practice is like at present, what are its rewards and disappointments, duties, opportunities, limitations, pitfalls, and dangers, how to enter (or try to enter) it, and what to do or not to do when in Though he by no means eschews detail, he is concerned at bottom with principles His guide is obviously the fruit of experience and thought, and it may be commended to all who either wish or ought to know more than they do about general practice and general practitioners in this country today

## Amputations

LEON GILLIS, M B E, M B Witw'srand, M CH ORTH Lpool, F R C S, consultant orthopædic surgeon, Queen Mary's (Roehampton) Hospital, London London Heinemann Medical Books 1954 Pp 431 84*s*

ORTHOPÆDICS already covers a larger field than "general surgery," and is subdividing into specialties Mr Gillis intends to produce a companion volume on artificial limbs and thus to cover all the problems which arise in amputees and those about to lose a limb He writes with the authority which his experience at Roehampton warrants, and this is certainly the most comprehensive work on amputations yet produced in this country

By its very scope it has involved the author in some difficulties He has included descriptions of conditions which may eventually give rise to the need for amputation, and his survey of the pathology and clinical course of so many diverse diseases is superficial and sometimes unsatisfactory Where he restricts himself to the immediate problems of amputations and amputees he is full of wisdom which will help every orthopædic surgeon

Particularly valuable are the chapters on amputations in children finger amputations, phantom limbs, and other complications which can affect the stump He has a good opinion of Syme's amputation when properly done, and recommends disarticulation at the knee as an excellent operation where indicated in children He agrees with general opinion in decrying guillotine amputations in emergency surgery, but he only refers in passing to the procedure of fashioning flaps and retaining them in position by a single suture over a generous gauze pack which was found so valuable by forward surgeons in the 1939–45 war

The book has many well reproduced illustrations, though some of the radiographs are too small to show the point at issue Doubtless many of the references were inserted to make the list complete, but a bibliography of over fifty pages seems excessive in a book of this size

This helpful book is to be highly commended to all who have to make the onerous decisions which amputation surgery involves

## Roentgen-Diagnostics

Vol IV *Gastrointestinal Tract, Gynecology, Urology* H R SCHINZ, W E BAENSCH, E FRIEDL, and E UEHLINGER Translator and editor JAMES T CASE London Heinemann Medical Books 1954 Pp 4029 £15

THIS is the fourth and final volume of this ponderous work on X-ray diagnosis Like its predecessors it has beautiful illustrations and a patchy, and at times uncritical, text

In general, the common disorders which face the practising radiologist and the student are all extremely well and elaborately described and in this particular volume the accounts of the biliary and renal tracts are first-class It is depressing however to find pages on gastric tone and gastritis, ve[illegible] ively little on hiatus hernia The appearances [illegible] mer Vinson syndrome and cricopharyngeus [illegible]

spasm get only a paragraph, while Evans's view of [illegible] arrhythmia as a cause of cardiac pain is accepted [illegible] question In places the clinical and pathological [illegible] not properly correlated with the X ray findings [illegible] the student to think when he reads that the [illegible] involved in 90% of cases of pulmonary tubercul[illegible] frequently in the early stages ?

The translation is a literal one and in places [illegible] from the verbosity of the original language The volumes cost £60 Much will stand the test of [illegible] much will be obsolete in ten years The trouble [illegible] an expensive production is that its cost almost [illegible] another edition within a reasonable period

## A History of Medicine

Vols I and II RALPH H. MAJOR M D, pr[illegible] medicine and of the history of medicine, Univ[illegible] Kansas Springfield, Ill Charles C Thomas [illegible] Blackwell Scientific Publications 1954 Pp [illegible]

THOSE who know Professor Major's *Classic D[illegible] of Disease* have been looking forward to the pu[illegible] of his history of medicine We are now more th[illegible] in his debt, for it is a splendid piece of work It [illegible] primarily to interest medical students and doctors [illegible] history of their profession, "which despite atta[illegible] abuse, despite quacks and charlatans, and in spi[illegible] own mistakes, has proved itself more enduring th[illegible] of the civilisations which gave birth to it"

Professor Major describes the development of th[illegible] art from prehistoric times to the middle of the 20th [illegible] from the days of the *Pithecanthropus erectus* of [illegible] lived some 500,000 years ago, down to the dis[illegible] cortisone His method is to describe the main [illegible] medical history in a connected narrative, and add [illegible] of each chapter a biographical section where the [illegible] find details of the lives of those whose achievemen[illegible] discussed The descriptions of developments in diff[illegible] ical schools during limited periods are particularl[illegible] for example, there are admirable sections on the [illegible] the Irish schools and the Great Men of Guy's during [illegible] half of the 19th century The four hundred (often [illegible] illustrations add greatly to the interest of the book and [illegible] many points which would be obscure from a descrip[illegible] Some are from photographs taken by the author [illegible] various parts of the world

Professor Major's interest in medical histo[illegible] from his student days when he came under the [illegible] Osler He shows himself a born writer, and his [illegible] one of the best and quite the most readable of the [illegible] histories of medicine It is a pity that its pr[illegible] prevent it from reaching the hands of most of our stu[illegible] but it is worth every penny Contrary to the [illegible] expectation it will also appeal to medical histori[illegible]

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**Any Questions ?** (Third series London Britis[illegible] Association 1954 Pp 227 7*s* 6*d* )—"I have answer[illegible] questions, and that is enough," snapped old Father [illegible] at his importunate offspring Happily no arbitrary [illegible] been imposed by the *British Medical Journal*'s team of [illegible] In this latest series their readers' obstinate ques[illegible] some 200 of them—relate to such diverse topics as [illegible] of the Mouth after Alcohol, Head wagging and Head[illegible] in Children, and the Dangers of Aluminium Weldin[illegible] reply embodies sound, practical advice, presented [illegible] that adds pleasure to the assimilation of new know[illegible]

**Sexual Disorders in the Male** (4th ed. London [illegible] 1954 Pp 260 18*s* 6*d* )—Mr Kenneth Walker and [illegible] Strauss, in this new edition of their book, have om[illegible] chapter on the surgical treatment of impotence, wh[illegible] felt had become obsolete, and replaced it by a [illegible] chapter on the concepts "male" and "female," exa[illegible] the temperate light of physiology, psychology, and [illegible] pology It could be read with advantage by all wh[illegible] to ignore the fundamental likenesses and the comple[illegible] rôles of the sexes Otherwise the useful little book [illegible] the same

**Stieglitz's Geriatric Medicine** —An English editi[illegible] book, which was reviewed in our issue of Nov 27 ([illegible] has now been published by Pitman Medical Publis[illegible] and the new English price is 90*s*

THE LANCET

*LONDON SATURDAY JAN 22 1955*

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## Cervical Spine and Nervous System

HE *neurological manifestations* of changes in the ical spine have received much attention in the . fifteen years but there is still a good deal of usion both about the *nature of the bone disorder* about the mechanism of the resulting neurological ects This confusion is reflected in the varied ication of such *terms as spondylosis osteo-* ritis disc protrusion, and degeneration of the e At first, workers were intent primarily on blishing the existence and character of the neuro cal syndromes due to abnormalities in the cervical e Following the lead given by Sir **RUSSELL** IN in his careful and thoughtful articles,[1 2] many rvers have added to the detailed descriptions of neurological patterns arising from involvement he cervical nerve roots.[3-5] Furthermore, both IN[1 2 4] and other workers including **SPILLANE** LLOYD,[6 7] have described the many different ifestations of changes in the spinal cord that may ound, and on p 171 of this issue Dr **CLARKE** rs attention to the frequency of this 'cervical lopathy'

he neurological effects of spondylosis are deter ed almost wholly by anatomical factors, and onal treatment must depend on correct apprecia of the anatomical derangements. The lack of nimity on the management of cervical radiculo- ny and myelopathy clearly reflects prevailing rtainty about pathogenesis The shadow of ilation of the lumbar intervertebral discs as a e of sciatica casts itself over all thought relating the cervical region, even though **FRYKHOLM**[5] ited to some very important differences between lumbar and cervical regions and remarked on the tive infrequency of soft nuclear herniations in the ical region Professor **CAVE**, Mr **GRIFFITHS** and **WHITELEY** in an article that also appears this k emphasise the importance of osteo-arthritis of neurocentral joints of Luschka in the production oot symptoms One very interesting feature of e of their cases was the absence of abnormality he disc space when osteo-arthritis of [illegible] ts was displayed radiographically *This finding* suggests that disc degeneration is not a sine-qua non of cervical osteo-arthritis, although the two often co-exist Not everyone will agree with the implication that radiculopathy is due rather to this osteo arthritis than to lateral herniation of the disc, but the observations and excellent illustrations give additional point to the view that many different factors may bring *about the neurological end results of cervical spondylosis* From published reports cervical spondylosis emerges as a pathological miscellany in which the *various subdivisions* may *be related both in nature* and in development The spinal abnormalities affect the cord and roots by pressure either on the nerve *tissues themselves* or on their nutrient blood vessels as **LIVERSEDGE** et al[8] suggested, and fibrosis of the root sleeve may play a part in the radicular symptoms[9] This pressure ischæmia may be aggravated by continued movements of the spine[10] It follows that therapy should be directed towards removing any or all of these factors, and will vary with the nature, duration, and extent of the skeletal lesion Here dogmatism still has no place, but it does now seem possible to lay down certain guiding principles for the management of the various types of disorder

It is quite clear that soft protrusions of the cervical discs may follow trauma and produce immediate symptoms ranging, according to their size and location from acute brachial neuritis to complete paraplegia or quadriplegia Such *symptoms* if severe enough require early operative relief for the removal of pressure In a sense this type of lesions is outside the bounds of cervical spondylosis But in some cases the initial symptoms subside with rest and perhaps by conservative remedies while in others the protrusions cause virtually no symptoms and in either event the stage is set for the later calcification of the protrusion, osteophyte formation, and the subsequent picture of the "single-disc" type of spondylosis noted in 18 of the 38 cases described by BRAIN et al[2] If these effects of trauma involve two or more levels—as they may—the ultimate picture may resemble radiographically and neurologically the full scale degenerative type of spondylosis *In this type of* case removal of the source of pressure on the cord might seem the ideal remedy but wrestling with an *ivory hard bar or knob in the vicinity of the highly* vulnerable cervical cord can be most unrewarding for surgeon and patient alike The presence of abnor*malities at more than one level*, particularly if demonstrated on [illegible] seems to contra-ind[illegible] direct approach to the [illegible] lesion but in [illegible] cases there is something to be said for la[illegible] even though the final results of such [illegible] still unknown Alternatively the [illegible] [illegible] weeks or months of a collar [illegible] [illegible] or plaster will alleviate or [illegible] symptoms but [illegible] like [illegible] [illegible] [illegible]

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[1] ain W R. *Proc. R. Soc. Med.* 1948, 41 5 [illegible]
[2] ain W R. Northfield, D Wilkinson, M. *Brain*, [illegible] 75 177
[3] ncet 1952, ii, [illegible]18
[4] ain W R. *Ibid* 1954 i 857
[5] ykholm R. *Acta chir scand.* 1951 101 [illegible]
[6] illane J D Lloyd, G H T *Lancet*, 19[illegible]
[7] illane J D., Lloyd, G. H T *Brain*, 195[illegible]
[8] [illegible]
[9] [illegible]
[10] [illegible]

The factors other than disc protrusion that may influence the final picture of cervical spondylosis are becoming a little clearer PALLIS et al [11] investigated 50 hospital inpatients over the age of 50, and detected narrowing of the spinal canal in three-quarters of this total, and narrowing of the intervertebral foramina also in three-quarters, but such spondylotic change was not always associated with neurological abnormalities In some cases these affections may have originated in a disc herniation of one sort or another, but shrinkage of disc spaces, not necessarily accompanied by actual herniation, and osteo arthritic changes of the cervical spine seem to be included in the price to be paid for longevity There is, it seems, an osteochondrous degenerative process ranging from generalised osteo-arthritis (with spondylosis from top to bottom of the spine) to the more localised affection of the neurocentral joints now described by Professor CAVE and previously mentioned by PALLIS et al [11] The neurological consequences of this type of spinal disorder are similar to those of the chronic spondylosis related to disc protrusion, and sometimes both factors may operate in a single case It follows that the management of this type of case will be similar to that of the spondylosis resulting from disc protrusion, with a more definite tendency towards conservatism Professor CAVE suggests that neurocentral apophysectomy of the affected joints is the only means of permanent cure for the lesions he describes, but as he himself hints, the technical difficulties seem insuperable If more than one abnormality is revealed radiographically, unroofing of the theca by laminectomy is similarly of doubtful value It seems, then, that application of a collar is likely to be the only means of alleviating this condition, and here again radicular manifestations will be more amenable than those of myelopathy Manipulation and traction and even "reablement exercises" may aggravate any or all of the neurological symptoms in these cases, and in this connection we may recall Sir CHARLES SYMONDS's [12] account of the rôle of trauma, or even ordinary movements, in precipitating neurological disabilities in the patient with cervical spondylosis It has been suggested that the spine might be fused, either as a complete treatment or as an adjunct to laminectomy, but the benefits of such action have not yet been clearly established Meanwhile it behoves us as we grow older to adopt a more regal posture and bearing, and to avoid all rapid, undignified movements of the head and neck, if we are to escape the manifold dangers of radiculopathy and myelopathy

Our new awareness of the frequency of cervical spondylosis brings in its train an important clinical responsibility Many neurological diseases may be simulated by cervical myelopathy and radiculopathy due to spondylosis, but there is always a danger that such another disorder may be present in a patient whose cervical spine is radiographically abnormal If the intrinsic neurological disease were itself degenerative or untreatable, the confusion with spondylotic myelopathy would not be of great practical importance But if the second lesion were, for instance, a benign tumour of the spinal cord or subacute combined degeneration of the cord, the attribution of symptoms to the coincidental spondylosis could be tragic

## Group Discussion

IF the aim of popular education is to create
informed, stable, and contented society, then
admit that so far the results have been disappo
Ignorance and prejudice, the two forces of evil
the educational reformers of last century so
siastically sought to overthrow, still estrang
from man and nation from nation The rea
course, is that the art of living with one's
cannot be learnt from textbooks, and knowl
chemical symbols or arithmetical equations help
in a world in which the most potent influ
unpredictable human nature

But let us not condemn education too pr
Its success, like that of the surgeon's knife, d
upon how it is applied, and if an operat
unsuccessful, the surgeon does not blame his
At its highest, education may unquestional
much towards improving human relationships,
are we justified in accepting that its best meth
application is the traditional one of "did
teaching ? Many experienced teachers believe
the traditional system the pupil's rôle is too p
to lead to any significant changes of attitude
process of learning, they say, is carried out pr
only if the pupil is actively coöperating, an
method they increasingly employ is one where
form small discussion groups, and where the
assumes to some degree the functions of a
This system has been successfully put into p
not only with students in schools and unive
but also with groups of people anxious to lear
to deal with the perplexing situations of dail
The principles and scope of the method are des
in a symposium published lately by the Central C
for Health Education [1]

As the introduction to this symposium point
the use of discussion as a means of teaching d
least from the time of SOCRATES Of late, how
the scope of discussion has been greatly widened,
its value is now recognised in fields which are
primarily instructional In youth clubs,
centres, and evening classes—in fact wherever
groups of people with some common interest
brought together—the method may be used for
everyday problems, and to reach a unanim
acceptable decision on future action For exa
parents may meet in their school hall and, wit
headmaster acting as group leader, consider
question of their children's home-work—how
should the children be required to do, and to
extent should they have help from their parent
a number of nursing mothers may, with gui
from the doctor of their infant-welfare centre, d
the subject of "clock feeding," and by pooling
experience decide upon some definite future p
As one writer puts it, "The process of reach
decision by discussion greatly enhances the c
of its being put into practice This is partly
no doubt, to a sense of loyalty to the group bu
to a sense of individual security in doing some
which is accepted by other people" For t
discussion to be most effective the number of p
pants should be small, the atmosphere informal

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[11] A. M Spillane J D *Brain*, 1954, 77 274
[12] *Lancet*, 1953, i, 451

[1] Group Discussion in Educational, Social and Working Life
lished by the Central Council for Health Education, T
House London W C 1 Pp 92 3s 6d

group leader someone who can guide the argument otrusively but firmly towards a definite decision re possible, the leader should have special know o of the topic under consideration thus a local ly doctor might preside at a discussion on The of the Elderly, or a local magistrate at a dis ion on Juvenile Delinquency It is important he should be able to put the members of the p at their ease and make each participant feel his contribution is valuable and interesting etimes, as one writer says, his function is merely merge the group and disappear —since the ussion may proceed even more energetically in absence But usually it is helpful if the leader s up at the end of the meeting, and formulates in le terms the proposed course of action.

the past twenty years the principle has been with singular success in psychotherapy, and oup psychotherapy is now a recognised way of ing some mental disorders At first sight there s to be little resemblance between a psycho apy group and a group of persons meeting to ider a difficult social question The latter attend heir own initiative, and have common interests aims The members of the psychotherapy group he other hand are selected arbitrarily by the hiatrist, often they meet as complete strangers they seldom have anything but their illness in mon Yet fundamentally the purpose of the groups is the same both overcome their diffi es by sharing them, and both gain strength from realisation that their troubles are not unique e psychotherapy group the patient " re-discovers ationally the home-spun truth, that in helping s, he best helps himself ' And that after all principle which applies to every section of society

## Recording Alimentary Movement

JR knowledge of stomach and bowel movements an is imprecise partly because no permanent l record can be made, unfortunately man has he transparency of the telescopic fish *Carassius us* Most investigations into the activities of the ntary tract have been biochemical and chemical in consequence our minds are trained and even ed, to the idea of chemical or hormonal causes of ic ulceration—the very term peptic denotes limitation Yet the constant location of duodenal in the first part of the duodenum suggests that echanical force with which chyme is ejected from ylorus may play a part it would be instructive o a ciné film in slow motion of a barium meal

e pioneer of X ray cinematography was MACIN [1] who in 1897 demonstrated the movements of g s leg on 40 ft of film He used both the direct indirect methods

the *direct method* a strip of X ray film is later graphed on to ciné-film By this method BARCLAY [2] found that initial filming at the maximum rate of mes per second [3] caused much vibration owing to eight of heavy moving parts and they had diffi in interrupting the electrical current at such short als since contactors for X ray apparatus are ally constructed for heavy currents and are therefore too cumbersome for rapid work The method was used for investigating circulation in animals and it should therefore suffice for the slower movements of the alimentary tract. With patients X ray dosage is a real problem, though the dosage can be curtailed by means of intensifying screens, which utilise the fluorescent effect of X rays on such substances as cadmium tungstate thus the proportion of film darkening due to X rays can be reduced to 2% the rest being the result of light rays stimulated by the X rays on the screen

Paradoxically the *indirect method* seems more direct The photograph is not taken direct on to X ray film; instead ordinary pictures are taken from a fluorescent screen REYNOLDS [4] made this method practicable by his device for turning off the X rays when the film was being moved and by using a ciné-lens of aperture f/085 But the X ray milliamperage must be high to obtain sufficient fluorescence, and if injury from irradiation *is to be avoided the exposures must be brief*; REYNOLDS limited exposure of any one area to 10 seconds

In man therefore these methods are cumbersome expensive and potentially dangerous But now with image amplifiers much greater brightness is achieved with smaller doses of X rays and so more protracted exposures are feasible These amplifiers convert the energy in which the image is cast from light on the fluorescent screen to electron emission from a photo electric surface These electrons do not radiate in all directions in the manner of light so almost the whole emission can be amplified and drawn by a positive pole through electrostatic fields which concentrate and focus them on to a small target screen where they are once more converted into light this is photographed on cine film and passed through a telescopic system for simultaneous direct vision Clearly the length of the amplifier tube is directly related to the size of the output screen the bigger the screen, the longer is the vacuum tube, and the more difficult is the apparatus to construct Accordingly screens have been limited to 5 inches square which is just too small for study of the alimentary canal in the adult but it cannot be long before these mechanical difficulties are solved The gain will be great for unit time of exposure the X ray milliamperage required is reduced two hundred times and according to COLTMAN [5] brightness can be amplified five hundred fold—which brings the image out of the region of rod vision into that of cone vision, where stereoscopy is possible

So much for direct visual recording of alimentary movements Much has been done in the past by way of indirect analysis of peristaltic and pressure waves The balloon and tambour system recording on a kymograph is attractive because of its simplicity its limitations have been overlooked A balloon is a shape unnatural to the alimentary tract the physiological response which it engenders and then records is unlikely to be related closely to normal waves of contraction From the physical aspect the system is most unsatisfactory, nobody would consider using a closed balloon tambour system for anything but registering contraction waves but even in a balloon/water manometer system the pressures recorded are not directly intraluminal since the size shape volume and elasticity of the balloon influence the pressures passing through the system [6] For recording contraction and pressure waves the intraluminal portion of the system must be small in bulk to avoid recording an alimentary response due to the apparatus, **ABBOTT** et al [7] devised a system of small metal capsules, each containing a flexible diaphragm carrying an electric contact which closed at known pressures The method was ingenious but complex, but it does indicate that strain gauges could perhaps be useful **BRODY** et al [6] measured pressure changes with an open tube in the gut and an optical manometer, the mass introduced was small, and the inertia within the system very slight

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[1] ntyre J *Arch Skiag* 1897 1 3

[2] clay, A. E., Franklin K J Prichard, M M L. *Brit J adiol* 1940 13 227

[3] de Maele M *Fortschr Röntgenstr* 1937 56 120

[4] Reynolds, R. J *Proc R Soc Med* 1934 27 [illegible]

[5] Coltman J W *Radiology* 1948 51 359

[6] Brody D A Werle J M, Meschan, I Quigley J P *Physiol* 1940 130 791

Motility has been investigated by the even less direct method of measuring electrical potentials **ALVAREZ** [8] applied electrodes to the thin abdominal wall of a small old woman and compared the gastrogram with visible peristalsis At that time he could use an intragastric electrode only in patients with achlorhydria, on account of the voltage variations set up, in others, by fluctuations in the level of acid in the gastric juice bathing the terminals Using non-polarisable electrodes, one in the stomach and one on the skin, **ADAIR** and **GOODMAN** [9] found a difference of potential (the stomach being negative to skin) which increased after milk was ingested Later in experimental work with **QUIGLEY** and **BARCROFT**,[10] these workers came to the conclusion that th potential did not depend on the pH of the contents or on activity due to secretion or m **ALVAREZ** and **MAHONEY** [11] had already d changes in potential at times when no [illegible] could be observed Now **MORTON** [12] has dev an electrogastrograph on which he records current due to secretory activity with sup alternating current due to action-potentials from motility He uses the same system of non-p sable monopolar electrodes with the active p the stomach, placing the independent el the skin over the right delto pectoral groove r shoulder, and he believes that the total of built up at cellular and tissue interfaces, which barriers to diffusion between the two terminals be nearly zero and can therefore be ignored. H hopes that these methods may make clear the nism of motility Both he and **GOODMAN** [13] him have diagnosed early carcinoma of the from the form of the tracing, and **MORTON** ha demonstrated variations from normal pattern presence of peptic ulcer, and has differentiated b gastric and duodenal ulcer These empirical f suggest that the electrogastrograph may prove in clinical practice, but the method is still experimental stage

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[7] Abbott W O Hartline, H K, Hervey, J P Ingelfinger, F J, Rawson A J, Zetzel L *Amer J med Sci* 1940, 199, 879
[8] Alvarez, W C *J Amer med Ass* 1922 78, 1116
[9] Adair G S, Goodman, E N *J Physiol* 1936, 87, 35P
[10] Quigley, J P Barcroft, J, Adair, G S, Goodman, E N *Amer J Physiol* 1937 119 763
[11] Alvarez, W C, Mahoney, L J *Ibid*, 1922 58, 4
[12] Morton H S *Ann R Coll Surg Engl* 1951 1
[13] Goodman, E N *Surg Gynec Obstet* 1942 75 5

# Annotations

## PALLIATION IN CANCER

DESPITE heartening progress in the treatment of malignant disease there are still many patients with cancer for whom there can be no cure The management of each one of these has its own peculiar difficulties, but it is clear from a discussion, on Jan 5, by the section of surgery of the Royal Society of Medicine that there is a wide choice of useful palliative techniques

The limitations of surgery in this field were clearly stated by Mr H T Simmons One of the surgeon's most valuable contributions is in the relief of pain by removal of the primary neoplasm, but the circumstances in which this should be attempted depend largely on his judgment and experience Incomplete excision of a tongue cancer can cause only harm, whereas in carcinoma of the stomach gastro enterostomy alone is most unsatisfactory In the small and large intestine the relief of obstruction by a by-pass is immensely valuable, but colostomy in an old man with an inoperable rectal cancer only adds another trouble and does nothing to relieve the distressing bleeding and tenesmus Mr H R Thompson has found, from the records of St Mark's Hospital, that 17% of a large number of patients submitted to what was believed to be a palliative operation were still alive 5 years later But often, said Mr Simmons, a heroic operation is planned and executed only to show the surgeon's audacity and technical skill Such an operation will be justified only if it brings considerable relief

Hitherto full advantage has perhaps not been taken of the neurosurgeon's power to allay pain There is a reassuring precision in spinothalamic tractotomy for painful lesions in the lower half of the body, and division of the glossopharyngeal nerve and of the posterior roots of the upper cervical nerves for intractable mouth tumours is less attractive only because it involves a [illegible] complicated cerebellar exposure But Prof N [illegible]t frankly admitted the shortcomings of leucotomy, which leaves the physical aspects of unaffected although the patient ceases to be by its ravages Respite is bought only at the flattening and shallowing of the whole personality No less important than the relief is the preservation of essential neural funct example, when vision is threatened by an int metastasis or the spinal cord by an osseous depo

Hormonal therapy is clearly valuable in the of cancer of the parasexual organs, but its effec in any particular patient is largely unpredictabl mounting experience of adrenalectomy has prov the benefit may be dramatic, although we must to balance the severity of the operation agai palliation achieved A preliminary report fr Murray Falconer suggested that hypophysect technically possible, and that in the hands of ex we can expect an acceptably low mortality Th of work, with its accompanying problems of replacement, should be confined to centres with facilities The suggestion by one speaker that the ment of every patient with inoperable cancer sh considered by a panel of experts, each of whom the limitations of his own technique as a palliati regarded by the meeting with some misgivi care of the patient might pass to a "muddle of d

Of drugs, morphine is our standby in the stages "it exists to be given and not merely to held" Nurses are often reluctant to give it in doses, even though the problem of addiction seldo There is too much persistence of the Calvinistic thought, which prompted Professor Dott to q Scots saying that "ye canna buy the grace o' dear" On the other hand, the patient will benefit if a diagnosis of inoperable cancer is made the justification for administering an its greatest merit is in the relief of pain and reserve it for this purpose There can be no har early and continuous use of analgesics, and speakers made a good case for administering chlo zine, especially when vomiting is intractable o burden of care of the patient in his latter days mainly on his general practitioner whose point of was expressed by Dr G F Abercrombie He lained that hospitals too often fail to tell their nts anything with the natural result that the general itioner is put at a grave disadvantage from the very t But it was clear from the later discussion that veryone would willingly follow his practice of always g cancer patients the truth He argued that we ly underestimate their ability "to take it" id been deeply impressed by their fortitude and ie mental adjustment that seemed to follow quite ully He saw nothing good in the dissimulation by r and relatives that must inevitably follow when rue diagnosis is withheld, and had never had good n to regret telling the truth In this regard we d campaign strenuously against the view so monly held by laymen that a cancer death is always ing and painful Dr P W Nathan took quite the ite point of view He felt that we have no moral to reveal the truth and that there is a good case for ultivated deliberate lie To judge by the views ssed by other speakers, the majority practice somewhere between the two extremes In the early the patient's powers of self deception are raged, and the truth is told only when the physician isfied that the patient wants it or when this seems in the interest of himself or of his relatives. By we may sometimes deny a responsible patient ly chance of putting his house in order Dr C J r wisely put the case for frequent visiting in such even when nothing overt is achieved often, there is a close bond of understanding between t and doctor there comes a time when the truth igh unspoken is equally revealed by an exchanged or a squeeze of the hand Mr Simmons deplored sual attitude of the surgeon who leaves the inoper ase to his registrar at the end of the list At no must the patient feel abandoned and the nurses and latives no less need constant encouragement

seems clear from this discussion that the choice thod will depend partly on the site of the tumour its natural history but even more on the patient's ter age and responsibilities and his position in

## STERILISATION OF SYRINGES

RY housewife knows that the hottest part of ing-oven is near the top Darmady and Brock,[1] y thorough experiments with ovens for sterilising es found a much higher temperature near the top linary electric ovens and this difference proved greater with two gas heated ovens An alternative d—namely boiling—was investigated by testing thermocouples the temperature attained by indi syringes; and it was found that if the syringe rapped in lint before being placed in boiling water was not reached for 5 minutes or longer The alternative—autoclaving—is unsatisfactory because ringes have first to be taken apart

rly if ovens are to be used for sterilising syringes hing must be done to equalise the temperature hout the whole space, otherwise the syringes near the top of the oven may be overheated while t the bottom may not be sterilised Darmady and therefore tested electric ovens in which the circula f hot air was aided by fans In such ovens the rature of the syringes provided that they were not d too tightly rose rapidly and evenly to the desired What this level should be seems still to be in e and the authors cite suggestions varying from for 1 hour (electric oven with fan) to 160°–180 C hours A report[2] issued by the Ministry of Health specifies 160° ± 5°C for not less than 1 hour Since spores of different organisms have different thermal death points Darmady and Brock suggest that an authoritative body should define the organism to be used for checking sterilisation by dry heat

From this valuable report certain principles emerge for those setting up a syringe service only electric ovens with fans are suitable the oven must not be overloaded with syringes, which must be packed loosely and the temperature of the syringe should be checked against the temperature recorded by the oven's thermometer Finally Darmady and Brock show that an electric oven with fan seems to work better if loaded while still hot—which is contrary to the M.R.C memorandum[3] and to the Ministry's report[2]

## THE HOME CARE TEAM

WE all know that far too many people knock on the door of the Englishman's castle and offer advice on health, infant welfare surgical appliances, housing drains school attendance delinquent behaviour tuberculosis mental ill health, and a variety of other topics and that no two of these specialists will necessarily give the same advice even when (as occasionally happens) they are talking about the same thing It has always seemed desirable to reduce their numbers and to have instead a few people with a broader outlook Some think that if the health visitor and the district nurse could have more scope and appropriate training they could with the family doctor take in most aspects of family life and that being already trusted family friends they are the right people to undertake this broad care

The opportunities for health teaching open to the district nurse working with the family doctor have lately been described by Dr J L Burn[4] medical officer of health for Salford Home care he thinks is bound to gain in importance psychological medical and financial reasons all favour the complementary use of the home and the hospital in the care of the sick Domiciliary visits by specialists—which he regards as one of the fine achievements of the National Health Service—have already enabled many people to stay out of hospital and have also ensured that many who need hospital treatment are admitted without undue delay This service in his opinion is being well and widely used in one region only in 1953 some 20 000 domiciliary visits were paid by consultants, and the numbers steadily increase Earlier discharge of patients from hospital is now being arranged in some areas though some hospitals—not confident of the standard of home care which now can (and should) be provided—hesitate to attempt it as a fixed policy If only one patient in twenty was discharged earlier, to the care of his family doctor and his district nurse it would greatly reduce the blockage of hospital beds and help the people on our hospital waiting lists

District nurses could be used more fully Dr Burn thinks in the care of sick children; these sometimes get less skilled nursing than they need—the nurse like the home help being expected to give her attention almost exclusively to old people Nor do pædiatricians get called in as freely as other specialists; and indeed the family doctor himself may not be called in till the last minute Such delays mean that some children's lives are lost unnecessarily Dr Burn urges that the health visitor should pay more routine visits to babies in "black-spot" areas and should press the parents to call in the doctor early when a baby is ill. She should also have far more official opportunity for collaborating with the district nurse who in turn should be in closer touch with the doctor All three—or their representatives—should have the opportunity of joining in discussions at the local health department when policy is being decided, and at Salford this is done

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[1] nady, E. M. Brock, R. B. *J clin Path* 1951 7 290

[2] ort f the Central Pathology Committee of the Ministry of alth on the Sterilisation of Hospital Equipment H.M.(51)118

[3] Medical Research Council War Memorandum no 15 H.M. Stationery Office, 1945

[4] *Nursing Times* 1954 50 11

The district nurse has "the unique and privileged opportunity" of being able to observe the whole needs of the families she attends, and she should be able, in his view, to call in, when necessary, the aid of the health visitor, the home help, the sanitary inspector, or any other useful person available under the N H S Some are already doing this, but a few, he hints, cling a little too rigidly to their prescribed duties He mentions the good spirit he found in the William Budd Health Centre at Bristol, where the health team—doctors, home nurse, midwife, and health visitor—worked keenly together in specially built premises According to them, "the most important room in the building" was the staff room, where they met daily to discuss their patients and their patients' families

The nurse's work, Dr Burns thinks, could be lightened if we employed less highly skilled people for some of the routine tasks—to give blanket baths, for instance We might also improve our supplementary services—arranging for "sitters up," making the loan of equipment easier, and providing laundry services for incontinent patients Another way of saving time would be for the public-health department to run a central syringe service, supplying doctors and nurses with all the sterilised syringes they need, and possibly with all other sterilised equipment Again, a daily clinic might be sponsored by the public health department, where the district nurse could give injections to all the ambulant patients on her list who needed them He mentioned, too, the opportunities both nurse and doctor have for health education, "supporting each other and encouraging the patients and their families in the promotion of health and the prevention of disease"

## EPITHELIOMA CUNICULATUM

The recognition of a new pattern in disease is one of the satisfying features of experience in the practice of medicine Such a piece of knowledge has been put on record by Aird and his colleagues [1]

They found, in a man aged 64, a tumour of the sole of the foot comprising an irregular bulbous mass of a curiously "squashy" consistence, on pressure greasy, foul smelling, "tooth-paste" material was expressed from the mouths of a series of sinuses, each opening on the top of one of the bulges Although the tumour had penetrated through between the metatarsals to present on the dorsum there was no hint of destruction of bone or of tendons—an impression which was confirmed when a sagittal section showed it to be a well defined tumour expanding into the soft parts The histological picture was exceedingly confused The tumour was made up of a complex pattern of anastomosing tracks, each lined by squamous epithelium and full of degenerating keratin It was no surprise that a small biopsy fragment led to no clear understanding of the orientation of the various cell layers A precisely similar clinical and histological picture was later found in a second case, again in the forefoot of an elderly man, and a third matching specimen was collected from the shelves of a pathological museum

From a study of these three cases Aird et al conclude that the lesion is a well differentiated squamous carcinoma of low malignancy which is modified by pressure Walking, it is presumed, forces the tumour up into the soft parts, in a manner reminiscent of corns and of plantar warts, and here keratin accumulates in cystic spaces which later empty through sinuses, to leave a distinctive soft and bulky tumour mass Aird et al believe that this form of squamous carcinoma is peculiar to the foot, and for it they suggest the descriptive term "epithelioma cuniculatum," from the resemblance of the tracks to the burrows of a warren There was no evidence of distant metastases, and treatment each case by amputation

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[1] Johnson, H D, Lennox B, Stansfeld, A G Brit J 51 42, 245

## PHYSIOTHERAPY EXAMINED

The tremendous medical advances of the pa years have included no outstanding innovatio field of physiotherapy In the late war a small e getic group of remedial gymnasts was formed Services, and the introduction of its methods into hospitals has marked a shift from passivity to a by the patient in treatment On the whole, b physiotherapy has latterly tended to be one of th conservative branches of medicine, and las Tegner [1] boldly called for reconsideration of the several forms of treatment whose worth has too often been taken for granted This enth borne fruit, for on Dec 8 the section of physical m of the Royal Society of Medicine met to discuss t and Abuse of Physiotherapy, and, in her remarks, Dr Doris Baker, president of the sectio that this was the natural answer to Tegner's ch

Dr A C Boyle pointed out that much of therapy is directed at painful conditions of the lo system, some of which are apt to clear up of th accord Physical methods, which are commonly sive, must not be prescribed as a mere placebo rest, and activity might each be beneficial, and c planned physical treatment had a place in certain pulmonary diseases, and neurological d —though even in these conditions much treatm was at present being applied was useless Sq Leader C B Wynn Parry went so far as to re gether microwave diathermy, ultrasonics, and m and he thought that the claims made for t constant current treatments, short wave di massage, and ultraviolet irradiation were exces that these remedies were grossly over prescribed emphasis of Dr A T Richardson's remarks w particular contribution that the specialist in p medicine can make to diagnosis and prognosis his knowledge of electrical changes Dr G O found that ultraviolet irradiation had a limite in dermatology he regarded the prescription of therapy in peripheral-vascular disease as quite unj Dr F S Cooksey welcomed the scientific inte that was now going on, and strongly advised the therapist to abandon out of date methods of tr and follow the medical profession in its scientific Finally, Dr W R Grant described physiother drug of addiction

It will be seen, therefore, that members of this section are by no means backward in scrutin forms of treatment which, during the years, ha allowed to claim what was probably too large a the practice of physical medicine

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[1] Tegner, W S *Proc R Soc Med* 1954 47,

Dr H K Waller, well known for his clinical on breast-feeding, died on Jan 15

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# Special Articles

## THE INCIDENCE OF
## CANCER OF THE LARYNX
### LATION TO THE INCIDENCE OF CANCER OF THE BRONCHI

JAMES MAXWELL
M.D Lond. F R C P

will refuse to admit that there has been a great
e in the incidence of cancer of the lung or
ial carcinoma within the past thirty years and
blem of this disease has acquired an added urgency
e of the suggestion that this increase may be
related to the rise in consumption of cigarettes
the same period. It is not always remembered
er that this question of the action of inhaled
t substances upon the mucous membrane of
spiratory tract has been mooted for a long

ongst the first to suggest that the inhalation of
t substances was a possible cause of bronchial
was Duguid[1] who in 1927 reported a high
tion of cases in outdoor workers Two years later
ell and Nicholson[2] discussed the incidence of the
ion and considered the possibility that amongst
factors, tobacco-smoking could be an important
At that time it was not even certain that the
was increasing in frequency and they confined
lves to the suggestion that if cigarettes were an
ant cause it would be reasonable to expect a
rtionate increase in females affected by this type
er, in view of the great increase in the number of
smokers at that time

933 Maxwell and Hogg[3] reviewed the incidence
yngeal cancer as revealed by the Registrar
l s figures over the twenty years 1911–30 It was
that the concentration of any inhaled carcino
substance would be higher when it struck the
*than when it reached the individual bronchi* and
erefore sought to discover whether cancer of the
showed the same apparent increase as cancer of
g Reasons were given for accepting the accuracy
figures used for a *comparatively superficial form*
gnant disease and the figures for cancer of the
gus and of the tongue were included for com
The results showed a slight increase in the
tion of cases of cancer of the larynx to cancer in
from 1·29% in 1911 to 1·92% in 1930 Cancer
œsophagus was found to have maintained its
tion whereas there had been a slight fall in the
ce of cancer of the tongue No definite con
s could be drawn from the figures quoted but it
ggested that the figures for laryngeal cancer
a useful basis for comparison for it was then
in whether bronchial carcinoma *was increasing*
uency or was merely being diagnosed more

*now certain that bronchial cancer has increased*
still increasing in frequency and the question
led carcinogenic substances has become a matter
nt importance both to the consumer and to the
of tobacco I have accordingly extended the
s investigation by examining a comparable series
es for cancer of the larynx in this country during
t ten years The results are set out in the accom
table figures for carcinoma of the œsophagus
he tongue being again included

It will be noted that cancer in general continues to increase steadily every year (There is reason to expect such an increase and the factors concerned have often been discussed) For cancer of the larynx however there has been no absolute increase in the annual returns for the past thirty years and consequently the proportion of laryngeal cases to the cancer total has actually fallen and indeed appears to be lower than it was before the 1914 war Cancer of the œsophagus shows a similar decrease and cancer of the tongue is becoming noticeably less common as the years go by

The increase in bronchial cancer is now universally admitted Yet the figures quoted here make it equally clear that cancer of the larynx is diminishing rather than increasing If the inhalation of carcinogenic substances is really an important factor in the production of bronchial carcinoma what can be the reason for this diminution? The main contact with any inhaled irritant must be in the larynx and the concentration of any such substance must be much less in the more distal parts of the bronchial tree Therefore if tobacco smoke or indeed any other inhaled irritant is concerned in causing malignant change in the bronchial epithelium the relative freedom of the larynx from cancer can be explained only by assuming that its mucous membrane is much less sensitive to the inhaled agent than is the mucous membrane of the bronchi Yet our knowledge of the action of most carcinogenic substances indicates that they act quite strongly on squamous epithelium and it would have been reasonable to expect that during a period when cancer of the bronchi has increased so considerably there would have been at least a perceptible increase in cancer of the larynx As there has been no such increase we must I *think conclude that whether or not tobacco smoke is a* factor in the production of bronchial carcinoma some hidden and hitherto unsuspected factor is responsible for the astonishing increase in cancer of the lung

TABLE SHOWING THE INCIDENCE OF MALIGNANT DISEASE OF THE LARYNX, TONGUE AND ŒSOPHAGUS IN ENGLAND AND WALES 1913–52

(The figures for 1911 1921 and 1930 are included for comparison)

| Year | Total deaths from malignant disease | Total deaths from cancer of | | | Percentage of all cases of malignant disease | | |
|---|---|---|---|---|---|---|---|
| | | Larynx | Œsophagus | Tongue | Larynx | Œsophagus | Tongue |
| 1911 | 35 902 | 462 | 1451 | 978 | 1·29 | 4·05 | 2·[illegible] |
| 1921 | 46 093 | 779 | 1907 | 1[illegible]5 | 1·69 | 4·14 | [illegible] |
| 1930 | 57 883 | 1117 | 2[illegible]00 | 1[illegible]10 | 1·9[illegible] | 3·90 | 2·09 |
| 1913 | 73 684 | 1027 | 2377 | 900 | 1·39 | [illegible] | 1·2[illegible] |
| 1914 | 73 497 | 993 | [illegible]196 | 912 | 1·3[illegible] | [illegible] | 1·2[illegible] |
| 1915 | 75 712 | 993 | 2268 | 802 | 1·31 | [illegible] | 1·06 |
| 1916 | 77 616 | 1010 | 2[illegible]63 | 75 | 1·30 | [illegible] | [illegible] |
| 1917 | 79 781 | 972 | 2352 | 7[illegible]0 | 1·22 | [illegible] | 0·91 |
| 1918 | 81 655 | 103[illegible] | 2311 | 718 | 1·2[illegible] | 2·83 | 0·88 |
| 1919 | 83 [illegible]01 | 986 | 2226 | 865 | 1·10 | 2·6 | 0·79 |
| 1950 | 85 270 | 991 | [illegible]316 | 671 | 1·16 | [illegible]·75 | 0·78 |
| 1951 | 86 080 | 1007 | 2340 | 647 | 1·17 | [illegible] | 0·76 |
| 1952 | 87 612 | 911 | 23[illegible]5 | 586 | 1·08 | 2·6[illegible] | 0·67 |

#### CONCLUSION

It is now certain that cancer of the larynx has not increased in frequency during the very period in which cancer of the bronchi and lungs has become very much more common It is difficult to understand why this should be so if the inhalation of a carcinogenic substance is a vital factor in producing cancer in the respiratory tract

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[1] d J B *Lancet* 1927 ii 111
[2] ell J Nicholson W *St Bart's Hosp Rep* 1929 101
[3] ll J Hogg J *Lancet* 1933 i 1081

# Medical Education

## THE FIRST FOUR YEARS

### A Plea for a Different and More Vocational Curriculum for Medical Students *

R A Q O'MEARA
M A, M D, Sc D Dubl, F R C P I, D P H
PROFESSOR OF PATHOLOGY IN THE UNIVERSITY OF DUBLIN

To produce beneficial results at student level, recommendations as to improvements in the methods of teaching must be very specific Generalities are of little value

The four years of which I am speaking here are the premedical year (which in Irish medical schools is still, almost invariably, taken in the medical school or university), the two subsequent years, devoted mainly to the study of anatomy, physiology, histology, and biochemistry, and the third medical year, in which the student devotes most of his time to acquiring some knowledge of pathology or basic clinical science in its various branches and to the study of materia medica, pharmacology, and therapeutics During this year, and also for a short time at the end of his second medical year, the student attends hospital and receives elementary clinical instruction, but it is not my purpose to discuss this part of his education, except in the most incidental way My object is rather to dissect the teaching which the student receives in preparation for his clinical years

The period is one of great importance, because it is during this time that the general education of the student should be completed in order to give him the stamp of an educated man, while at the same time he has to be provided with the necessary technical knowledge in the basic sciences appertaining to medicine Is it possible to give him the advantages of a broad general education, combined with a high standard of medical training, in the time permitted? I believe that it is, but to achieve this happy result many revolutionary changes require to be made in the methods of teaching

### THE NEWCOMER

In Britain, it is quite usual for the instruction required for the premedical examination, or its equivalent, to be given at school But it has been a great mistake to separate the premedical year from the rest of the medical course It is greatly to be regretted that the final years at school should be occupied exclusively in the study of chemistry, physics, and biology, with entrance to a medical school in view, when these years should in reality be spent in more general cultural instruction in languages, literature, mathematics, history, and geography, with chemistry, physics, and biology as possible alternatives to additional languages as subjects of cultural value in their own right

While at school, the student does not learn how to learn He receives instruction in classes from teachers who help him over the more difficult hurdles in the set course He comes to the university untrained in any particular plan of learning For the first time he is thrown upon his own resources and has to find his own level. There is no doubt that individuals vary enormously in the methods of acquiring knowledge which they find best suited to their particular mentality, training, and outlook After a time, many students probably work out a system for themselves which they find gives reasonable satisfaction, there are many others, however, who never acquire a learning, but proceed as best they can and b sheer hard labour, and very often unreasoning tion, learn enough to satisfy their examin successive stages of the medical course What here is an advisory system for students to them, preferably individually or alternatively i groups, how best they may go about learning the they have to assimilate during the coming yea method which each student finds best for his own ments should be well established by the en premedical year and should stand to him there the rest of his medical course and, indeed, of his career

At the beginning of the premedical course and subsequent course, the students should be told w have to learn and why they are learning it O many of them are completely at sea as to why th to study a given subject, how they have to stu to obtain the maximum return for their eff where it fits into the pattern of medical studie lead, ultimately, to medical practice A medical system is thus envisaged, whereby students instructed at an early stage how to go about the subjects they will be required to master relevance of the subjects of the curriculum to t of medicine

The student cannot be expected to grasp, the relevance to the theory and practice of the subjects in his premedical course and in courses in anatomy, physiology, biochemistry pathology He may well seem to be far from the of the patient, where he conceives his proper in emulation of the doctors he has known and the teachers whom he admires In many respects, great pity that his first visits to hospital are now deferred But if it were to be explained to him standing success as a clinician and the inner satis knowledge well applied are, in reality, depend the mastery of these earlier subjects—he would content with their study What we, who are with these earlier phases of his medical educatio to consider is the best method of imparting in so as to help the student to acquire the mastery

Commencing with the premedical year, durin the student receives instruction in chemistry, botany, and zoology, we can see an courses which are highly relevant to his futu medical student and as a doctor

### CHEMISTRY

It is difficult to understand why chemistry (t slightly less extent, physics) has been taken out medical course proper Historically, rational me founded on chemistry and anatomy With the em of chemistry from alchemy, advances first be made in our understanding of physiological As chemistry advanced, so also advanced our kn of cellular life, of fermentation, of pharmacol therapeutics, until today it is possible with the chemist to conquer infections, to relieve pain prolong life, not merely in belief but in dem fact

The teaching of chemistry has passed out control of doctors, who formerly did much of it to the growth of the science and its incre plexity, this change is perhaps inevitable M many aspects of chemistry which are of great im in modern medicine are to be found in the more parts of the subject which, normally, only honours students would be required to know circumstances, it may appear difficult to pro

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* Extracts from a presidential address given to the Dublin University Biological Association on Oct 30, 1954 The address appears in full in the January issue of the *Irish Journal of Medical Sciences*, and these extracts are d by courtesy of the Editor of that journal

n medical student with a course in chemistry at relevant and adequate and at the same time, ently simple. My experience in examining medical its in chemistry however, shows that they can e a highly competent theoretical knowledge of the t in a course which is not too long What is ed consequently is a clearly defined course on a standard textbook should be written

textbook would be like no existing textbook in stry and would be subject to frequent revision It give in simple terms the more important points in cal theory followed by a special treatment of nic chemistry based upon the periodic table e it would proceed to organic chemistry dealing in with the straight-chain and ring compounds and derivatives, from the point of view of structure ting the student with a consecutive and logical tion of the subject In both inorganic and organic stry selection of material for special mention would do in relation to its importance in medicine To xtent this has been done in the past, but there is time-lag between the recognition of the importance ne *aspects of chemistry in medicine and their* on in the premedical chemistry course. A similar ng tends to retain in the course as important to the nt many subjects which have long ceased to matter e instances from inorganic chemistry arsenic, and ormerly much stressed are now of little consequence other hand it is not many years since beryllium ntalum were mentioned in small print in quite large on inorganic chemistry but today each is of ance in medicine the first, because of its violently ve effects on the tissues; the second, because it nert The textbook would be further embellished ction on elementary physical chemistry in relation dicine, and would contain chapters written in opular style dealing with a variety of selected illustrating the importance of chemistry in ne.

h such a textbook the need for more than a few lectures would disappear and their place could be with advantage by tutorials and lecture demon ns to small groups Medical students should learn ro but they should be required to learn only a uations, those necessary for practical titrations urse of reactions could quite well be indicated by m showing the nature of the chemical change in n It is unnecessary to produce a balanced equa r the understanding of most reactions and in nstances, it is merely foolish since the equation ot *in fact* represent *the true course of the reaction*

student s studies in theoretical chemistry would pplemented by a practical course in which the sis would be upon those chemical procedures which kely to find of greatest use in his subsequent studies icine and in medical practice Thus he would do little qualitative analysis and that carefully d, but he would do many titrations so as to become ghly adept in the use of pipettes and other instru of chemical measurement In designing practicals r they be in chemistry or in other subjects one ear in mind their four fold purpose They serve n observation to train manual dexterity to aid derstanding of the theory of the subject and to t in the planning of experiments From the t s point of view the first three are the most ant

## PHYSICS

ing to physics the pattern observed for chemistry repeated There are many aspects of physics in general is a difficult subject on which special on could be focused from the medical point of view In any event one finds in teaching and examining students that those parts of physics which are relevant to their medical course and to medical experience are often forgotten

It is surprising how many students in their third medical year still do not understand the microscope and the way to use it to best advantage To cite another example when examining in hygiene one finds that few students understand the arrangements of the ordinary domestic hot water supply Involving as it does a knowledge of the elementary principles of hydrostatics, of conduction and convection of heat the hot-water supply of a house provides a simple practical example of the application of physical theory which is important to health It is in any event something which the doctor should know—if only as a family man, which most medical students are destined to become One may contrast the lack of knowledge of these simple but important questions with the advice once given to me by a predecessor of mine as examiner in physics to the effect that if information was slow in coming in the viva voce the question to ask was the laws of the transverse vibrations of strings This never *failed to elicit* a correct reply and the examiner and candidate parted on good terms The question was clearly a grinder s tip based on an imperfect notion of the importance of these laws to the functioning of the vocal cords

So in physics, as in chemistry what we require is a clearly defined course around which a textbook suited particularly to the needs of the medical student should be written The matter could be presented in such a way *that it did not lay too much emphasis upon the mathematical* approach to the subject which is that of the true physicist but is beyond the powers of the average medical student The elementary theory of physics and its practical applications in medicine could thus be made available in a relevant fashion supplemented by lectures and lecture demonstrations. As for practicals while some devoted to experiments proving the truths of physics may be desirable, however inadequately they maybe conducted by medical students it seems to me that much of the time devoted to practicals could be spent in becoming familiar with the working of instruments based on applications of physical theory, which are used in medicine and surgery To take a few examples when learning the theory of the screw should practical work not be directed to learning at the same time the uses of different types of screw how to thread a screw and so forth? And in optics once the properties of different kinds of mirrors lenses, and prisms had been *explained, the student might study the microscope*—taking a simple microscope to pieces and reassembling it Would it be absurd to suggest that he should start to use the ophthalmoscope the laryngoscope and similar instruments if not on the living subject, at least on models?

## BIOLOGY

Botany and zoology are subjects which linger in attachment to the medical course Each has its relevance but nowadays *it is mainly* to a *later phase* in the student s career than the premedical What is particularly needed at the early stage is a course in biology to explain to the student the nature of life starting with the smaller simple cells their elementary metabolism and mode of reproduction and from that proceeding to the more complex multicellular forms of life especially in the animal kingdom. This course should include an account of the differentiation of tissues and organs as one ascends the scale of life and of their functions An elementary introduction to the study of heredity and genetics should be included It is at a much later stage when the student is doing pathology that a short course [illegible] protozoology helminthology and possibly should be provided, together with some account of the pathogenic fungi

ESSENTIALS—AND EXTRAS

In the suggested approach to the preliminary medical subjects there is no intention of decrying the invaluable services to medicine which so many teachers in these subjects have rendered in the past and will continue in the future It would not be possible for them, in existing circumstances, to design courses along the suggested lines, since medical students have to be fitted into the general pattern of science instruction in the universities The proposed ad-hoc courses in chemistry, physics, and biology would require special staff and facilities My object is rather to suggest the adoption of the general principle that instruction of medical students in the subjects of the medical curriculum, during the first four years, should be regarded as technical instruction and that the content of the various courses should be adjusted accordingly As far as possible, this adjustment would lead to the adoption of set courses, in theory and practical work, considered adequate for the requirements of the average medical student, and on these courses the professional examinations would be conducted The operation of this plan would substantially shorten the time spent on professional studies and would enable the university to devote more time to the student's general education

The study of subjects of cultural value would occupy part of that time The subjects chosen would necessarily depend upon inclination and ability For some, perhaps, mathematics, for others classical or modern languages would be an attraction It is particularly desirable nowadays that doctors should learn languages First, there is the cultural value Whether the additional language studied be Irish, French, German, or one of the other European languages, the training is a cultural asset In addition, a language is an instrument of contact with our fellow men in other lands It is less easy for us, than for those who live on the Continent, to acquire a speaking knowledge of a language other than that which we normally use, but it becomes more worthwhile every day At medical conferences abroad, Irish and English delegates are noticeably far behind those of other countries in this respect

Again, the subjects of the medical curriculum in their wider scope are of cultural value With the teaching of these subjects for professional purposes restricted to essentials, there would still be wide fields for the more brilliant and enterprising students to explore Facilities should therefore be available for the pursuit of higher knowledge in any of these subjects by students who possess the necessary ability and inclination As a stimulus, particularly to such students, it is to be assumed that a programme of research will be in operation in all teaching departments

ANATOMY, PHYSIOLOGY, AND BIOCHEMISTRY

If we have delayed too long on the premedical course, it is because the subjects of this first year are well suited to illustrate the pattern of medical instruction as technical instruction During most of the next two years the student has to learn human anatomy, physiology, biochemistry, and histology One may claim at the outset that a sound relevant knowledge of physics and chemistry, gained during the courses suggested for the premedical year, would be a very great help in the study of physiology and biochemistry The courses would have been designed to prepare the student for the application of the laws, theory, and experimental methods of physics and [illegible]mistry to the living animal

[illegible] ay, however, is in a different category There is [illegible] tute in clinical medicine and surgery for an accurate knowledge of anatomy And such on which finesse in clinical diagnosis and sound in treatment so often depend, can only be obt the most diligent application Nowadays a real has arisen in the teaching of anatomy in man centres, owing to the shortage of subjects for d Without freely available facilities for dissection, to be expected that the student can achieve the of knowledge needed to enable him to place his will over the site of any structure in the body of or child and to indicate the approach to it Y the standard of anatomical knowledge which and surgical practice demands One is tempted t that the members of our profession should o as in the days before the passing of the Anat sign a pledge donating their remains after deat anatomists to be used for the proper instr students

Formal lectures to large classes in descrip systematic anatomy are of little value as comp lecture demonstrations to small groups Whe anatomy, however, one felt the need for a tory lectures to indicate the general design of and the nature and properties of its main system it would have been a help to know that the ske stitutes the framework to which the muscles a what muscles are and what they do, and th arrangements of the heart and blood vessels a nervous system Looking back on the early dissection, when one began what might b amateur exploratory anatomy in the region of t it would have made things easier to have know starting, the sort of things one had to look for, w came from and where they went

But no amount of knowledge of the position tures in the body is adequate without a their function , and the modern approach to the of physiology and biochemistry to medical directed primarily towards an understanding functions and requirements of the human, a from the animal, body has been a great a medical education It is bearing fruit, more a in the application of these sciences and their to clinical medicine One might be permitted the likewise that in the study of histology greater on the microscopic structure of human tissues would be an advantage A closer cooperation b pathologist and histologist might help to bring pathologists have access to relatively normal tissues and organs, as well as to those which a by disease The specimens at their disposal it is true, satisfy the more exacting requiremen normal histologist as to fixation and details o structure, but they are often sufficient for the of students in normal histology

CORRELATION AND INTEGRATION

The student requires to be told at interval subjects which he learns in some parts of t correlate with those of other parts In sugg many formal lectures should disappear, t being taken by lecture demonstrations and would also suggest that room should be made of correlation, for which there is a decided need lectures the student would have outlined to him he has learnt and is learning, and how the the programme and link up with other par course

At the end of the second medical year and third medical year, he attends hospital and be pathology or basic clinical science At the sa studies materia medica and therapeutics Unfo however, integration is lacking between diff pathology course on the one hand and between ction in pathology and clinical instruction on the The lack of integration between pathology and edical aspects of bacteriology and immunology is table, but the lack of integration with clinical ine and surgery is even more serious The difficulty in part because the medical student nowadays hospital attendance so late in the medical course ather meaningless for the student when he hears tails of pathological changes found in cases which s never seen. The demonstration of lesions in ens only partly fills the void, and many students reat difficulty in understanding clinical disease they have not seen in terms of lesions demon d to them in specimens

medical sciences have changed more in character athology during the past twenty or thirty years ly has there been a great increase in knowledge much which was formerly vague theory is now hed on a basis of solid fact but during this period pathological lesions formerly common have now ly or totally disappeared. Two things about gy are outstanding One, that it is a great of correlation. Dealing as it does with the causes se, as well as all aspects of the changes which ught in the structure and functions of the body se it occupies a central position linking the earlier s of the medical course to itself and to clinical e and surgery The other is that today it occupies ition of arbiter of diagnosis Modern diagnosis e made in terms of the underlying pathological diagnosis by signs and symptoms alone is not t Pathology is necessarily a subject of enorm ide scope and is inseparable from clinical medicine, ecially during the third medical year it lends being taught as a technical subject in relation to medicine and surgery Its teaching can be so ed that within the framework of general pathology y relevant body of knowledge may be acquired student

o the end of this year, the general education of lent should be completed so that he is now as tructed in his chosen field of arts or science as other students of the university For the remain his medical course his instruction is mainly a or his clinical teachers but in the plan which I tlined he will have been specially prepared by a elevant technical training and a good general n to assimilate the knowledge and skill which ready to impart

### OBJECTS OF EDUCATION

uggestion is often made that one of the chief in the medical student s education should be to to think for himself. I would venture to suggest dment—*that the aim must rather be to teach* hink correctly. For right thinking there are two , knowledge and a trained mind Both are ome of sound education which not only provides ge and teaches the way to add to knowledge acquired, but also trains the mind to weigh and nowledge to the best advantage Education oo highly specialised is incomplete and imperfect. n dangerous The doctor whose knowledge is to the science of his profession is an imperfect o matter how well informed he may appear to dical matters In order to be fully worthy of ition in the activities of his profession, the ust be not merely a scientist but also a man of and of wide and varied understanding To ributes he will in time, add experience and and thus come nearer to perfection in his

## In England Now

*A Running Commentary by Peripatetic Correspondents*

We realise we are under the dew-claws of our cats, but at times I think they go too far When we lived on the second floor they arranged to come in and out by way of a tree, which meant we had to keep the sitting-room window open to the elements night and day It was a hardy life, but we won through When we moved to the third floor they looked out disapprovingly, and intimated that there was no tree At enormous expense we had a cat-ladder built by a distinguished firm of ladder makers It was one plank wide with balconies at intervals and could have presented no difficulty whatever to any able-bodied cat Snug when deposited in one of the balconies, looked pleased and expectant; Flute on the other hand, gave his well know impression of Macbeth at the sight of Banquo s ghost Then they both required us to take them in again The ladder-builders were beyond praise they made it two planks wide with a handrail and enlarged the balconies Snug immediately toddled sedately down and Flute, after a bad attack of the vapours rushed down and up again but of course as soon as that system was working smoothly we moved again, this time to a house in the country

The kitchen window presented no difficulties to the cats, but having it constantl open covered us with chilblains and meant we never got a hot meal so we called in George to make us a cat door It was a new idea to George, but he took to it with enthusiasm. We came home at nightfall to find he had bored a porthole in the backdoor about 5 in in diameter and 8 in from the ground—nicely placed for a burglar who had only to slip his hand in and draw back the bolt Mrs S who does for us was very pleased with it I spent the whole afternoon, she said training me cats and at the end they was coming in and out lovely Whatever they did for Mrs S they were determined to make us suffer They looked from us to the porthole, put two paws and a nose through and stared into the night, and when gently chivvied from the rear lumbered through in an uncouth bone-rapping manner that put our hearts through the wringer We telephoned to George who awed by our remorse promised to come next day and enlarge it. ' And while you re about it, we said hang a bit of wood across the hole so that they can push it open from either side that ll keep out the draught.

Home we came at eventide to find he had been as good as his word. He had hung a stout billet of timber in the opening which, so the cats intimated was quite beyond their strength to move. He had also transferred the bolt to a position out of reach of burglars where it interfered with the latch of the door Working fast we anchored the billet of timber out of the way by means of two screw eyes and a bit of string thus leaving the cat-door in the permanently open position A strong blast straight off Greenland whistled through the hole and filled the house. The cats repeated their act of peering timidly out and finally making the supreme sacrifice of struggling through bumping their rumps on the billet as they went and leaving lumps of fur on the woodwork We went despondently to bed An hour later we awakened to a noise of galloping Investigation revealed two cats charging up and down the hall and taking the cat-door like race-horses tails streaming heels tucked up behind Beaming indulgently we tiptoed back to bed

• • •

I have always found ambivalent a difficult word to slip easily into a conversation but I think it could be applied to the feelings of Edinburgh graduates who read in the *Times* of Jan 15 that the senate of their university had refused to allow the students to use the McEwan Hall for the installation of their new rector Most of us are sorry to hear that another tradition has lapsed but the installation of the rector is one of the more robust academic occasions, and anyone who recalls the indignant squawks of a clutch of outraged hens let loose in a flurry of toilet-rolls from the upper galleries of the McEwan Hall will not be able to withhold a certain measure pathy from the senate especially as £15,000 been spent on the redecoration of the hall thoughts I should perhaps reserve ambivalent to describe the feelings of Sir Sydney Smith, the new rector, who as chairman of the senate meeting must surely have announced this inhospitable decision with regret—and relief

* * *

DISTINGUISHED FOREIGN COLLEAGUE May I bother you about a small point which has puzzled me lately? As you know, I follow English medical publications closely, yet I do not seem to have heard of any of the authors of a series of authoritative papers which is appearing in *The Lancet* Sir Daniel Whiddon, for instance, where is he a professor of surgery? And Dr Harry Hawke—which great laboratory does he direct?

ME (heartily) I don't wonder you were puzzled But the explanation is quite simple These people are not writing under their own names They have chosen pseudonyms

D F C What a pious custom. No doubt in this way they commemorate revered physicians from your glorious past Sir Daniel Whiddon and Dr Harry Hawke belong, with Harvey, Osler and Lister, to the history of British Medicine

ME Well, you might think so, but actually, though it may seem rather odd, they aren't doctors at all You see, they all used to live near Widdicombe

D.F C Ah, then they all perhaps held chairs at the University of Widdicombe—no doubt a famous medieval seat of learning

ME Well, not exactly In a way they did all have seats at Widdicombe, but it wasn't so much chairs as seats on a horse They all took part in a famous ride

D.F C Ah, I understand They were the heroes of some dashing heroic exploit Perhaps they brought the good news from Widdicombe to Bristol I can see that gallant cavalcade of horsemen

ME Well, actually it wasn't quite like that either You see, though there were eight men, they all rode on the same horse

D F C Eight men on one horse! But I thought the English were always kind to animals Who owned the horse?

ME They borrowed the horse—a grey mare, rather a large one, I fancy It's all described in an old song The first verse goes something like this

Herr Tom Pearce, Herr Tom Pearce
Leih mir Deine graue Stute,
Dann reit' ich entlang am Ufer des Lea
Und besuche den Jahrmarkt in Widdicombe
Mit Herrn Brewer, Herrn Stewer, Herrn Gurney
Herrn Davey, und Onkel Thomas, et al

There, that explains the whole set-up

D F C Y—e—s Perhaps there are other verses?

ME Well there are, but I don't think you'd find them very helpful

D F C At least tell me what they did at Widdicombe

ME Oh, but I don't think they ever got there

D.F.C But what hindered them?

ME (uneasily) Well for one thing, the Mare stopped to make her will

D.F C To make her will!

ME That's right, old chap You know I was afraid you would find this part rather confusing

D F C I suppose the Mare will be writing to *The Lancet* herself next

ME Well you know, I shouldn't be at all surprised if she did

D F C Perhaps a contribution on veterinary medicine

ME Well, actually, I think she's more likely to write and tell the others where they get off

D.F C (infected at last) With all eight on her back at once she has every justification!

* * *

'SURGICAL POLYPHARMACY'[1]

Disease and cure
Are oft obscure
Physicians in such
Cases prescribe too much,
And that heresy
Is called "polypharmacy"

Surgeons remove
When in doubt,
Sundry bits and prove
Man can do without
The knife, thus erratic,
Is "polypragmatic"!

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[1] See *Lancet*, Jan 8 1955 p 8

# Letters to the Editor

## ARGENTAFFINOMA AS ENDOCRINE

SIR,—You have twice[1] drawn attention to the endocrine function of argentaffinoma, in that carcinoid is associated with a syndrome manifested by flushing, right heart disease, distress, and diarrhœa. These manifesta attributable to release of serotonin (5 hydr mine) into the blood from the tumour This been supported by the preliminary demon hyperserotoninæmia in 2 patients exhibiting drome[2] You have also suggested that urinary 5 indole acetic acid (5H I A A)—the product of deamination of serotonin—might be increased in with malignant carcinoid and that a method assay might serve as a diagnostic test

We wish to report results of preliminary 3 cases of malignant carcinoid in which a recently developed method for assay of urine[3] In all 3 patients the daily excretion of was tremendously increased over normal contro

*Infusion of serotonin in control patients*—On received 31 mg of serotonin base over 60 minut other 10 4 mg over 30 minutes Both had local vein, and abdominal and bladder cramp when began or when the rates were increased. The hyperpnœa, and tingling and burning of the face during infusion There were moderate (11 and increases of mean arterial pressure Objectiv was flushed A wide experience with other pat serotonin by instantaneous intravenous injection that amounts of the order of 1 mg base are as m will tolerate because of the discomfort Urines we during and after infusion, and increments in 5H.I.A. were calculated by comparison with outputs other times The increment in the first patient over 3 hours and in the second 2 6 mg over outputs in other specimens were about 5 mg per Thus, the patients excreted as 5H I A.A. respec and 25% of the serotonin infused

*Malignant carcinoid*—Observations were ma patients One, a patient of Dr George Crile, jun., of Clinic, was an elderly man with widespread abd hepatic metastatic carcinoid, who did not exhibit the noid syndrome" Outputs of 5H I A A in his urine occasions were 65 and 230 µg per mg creatinine, or as many mg daily A biopsy of the tumour tissue for a rough bio assay in an anæsthetised dog, which a serotonin content of 0 9 mg per g of fresh tissue second, a woman who was flushing and had other istics of the syndrome, is under study by Colonel Mattingly, of the Walter Reed Hospital, Army Center, her urinary 5H.I A A was found to avera 350 mg per 24 hours Blood concentrations of were measured and found markedly increased ov The third case of malignant carcinoid, a patient of Dr Sampson, of San Francisco, yielded 142 mg of 5H 24 hours Clinical details of this patient are not at this time

These observations substantiate the sugge increased urinary 5H I A A is of diagnostic malignant carcinoid, The levels found in patients vastly exceed the 5–10 mg per 24 h in normal subjects,[4] or in a wide variety of dis

The infusion data indicate that less than circulating serotonin is excreted as 5H I A A, from seems that serotonin release in malignant carc range from 200 to 1000 mg per day or 0 1 to 0 minute

Attribution of the clinical syndrome to releas tonin alone is still questionable, since infusio

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1 *Lancet* 1954 ii 372, *Ibid*, p 958
2 Pernow, B, Waldenström, J *Ibid*, p 951
3 Udenfriend S, Weissbach H Titus E O To be
4 Titus, E O, Udenfriend S *Fed Proc* 1954, 13, 411

t rates of about 0 5 mg per minute did not repro ushing or other aspects of the syndrome Further, ic flushing was not detected in one patient (that Crile) during several days observation in the of which great urinary outputs of 5H I A A were ed. The estimates of serum serotonin by Pernow aldenström [2] indicate the instantaneous presence od of some 30 mg of circulating serotonin This te seems excessive It is much more than control subjects tolerate by instantaneous injection ly by analogy with phæochromocytoma the istencies can be resolved by demonstration of ice of the patients to very large amounts of the and by supposing episodic release thereof It assumed that current studies to which the material communication is preliminary, will unravel this nism. At least the data show that measurement iary 5H.I A A is of diagnostic value in malignant oid, even when as in one of these three patients nical syndrome is not apparent

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nic Foundation and
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nstitute of Health

IRVINE H PAGE
A. C CORCORAN
SIDNEY UDENFRIEND
ALBERT SJOERDSMA
HERBERT WEISSBACH

## PULMONARY EMBOLISM

—May I support Dr Aidin (Jan 8) in his plea for ent approach to the problem of thrombo-embolism? time ago [3] I put forward a hypothesis which was nconsistent with the work to which Dr Aidin and it is gratifying to find that doubt is again cast on the guilt of "venous stasis."

tories, the blood moves quickly in veins it moves less and in capillaries and sinusoids it moves very indeed. At the periphery of all vessels it is virtually ary and there is reason to believe that the blood in with the lining of the aorta is as still as the water anks of the Thames. It so happens that intravascular is most common in the arteries, and least common capillaries and sinusoids, but it does not follow that osis is the result of "arterial hurry"

esearch can be diverted into more profitable ls two advantages may accrue

The real cause of thrombo-embolism may be found ional treatment become possible

urgeons may refrain from chivvying their elderly s out of bed for a few minutes on the day after a operation I have often wondered what this astonishing supposed to achieve; the only tangible results I member are two apoplectic seizures and one acute failure

elieve that thrombo embolism may be related ding of the veins by products of the tissue kata which follows confinement to bed wasting disease, erative or other trauma This katabolic process a maximum about ten days after an "injury" ere is little evidence to suggest that the process modified by short term alterations in the diet— there is some evidence to the contrary

Mimms
ferts

A J DOWNIE

## RSENESS AND CORONARY THROMBOSIS

—The hoarseness noted by Dr Sarkany and dwood [4] as a sign of coronary thrombosis has been r to me for several years I do not think that it gn of coronary occlusion only; I have observed patients with no certain evidence of infarction I followed up for several years—though of course in these cases coronary thrombosis cannot be ruled out Laryngological examination never revealed any organic lesion I attribute the hoarseness to the exhaustion caused by severe and distressing pain

Hufeland Hospital
Berlin

R SCHEUER KARPIN

## THE BURNT CHILD

SIR —It is a pity that Dr Shannon in his excellent account last week of some of the aspects of the management of burnt children should sow jangling discord with his disparaging comment on physicians It is a pity that after looking at a burnt child he did not look further afield He might then have become aware of something of the contributions of physicians to the care of burnt children and learnt that there are physicians who have the training experience and outlook to help in these problems When the medical profession is being split into so many different specialties anyone who, by his written or spoken word creates factions and feuds is doing a disservice to medicine

Dr Shannon is of course right when he says that The custom of referring seriously ill patients to physicians for preoperative assessment is to be deplored There should be no question of reference the physician should be concerned with the child from the very first. Burnt children as other children are the better cared for when one or more of the team are familiar with the peculiar problems of childhood and are interested in their families and homes as well as their illness and Dr Shannon can be assured that the team that includes integrally a pædiatrician is more complete than that without

Newcastle upon Tyne

GEORGE DAVISON

## ADRENALECTOMY FOR HYPERTENSION

SIR,—Your excellent leading article of Jan 8 stimulates me to draw attention once more to the value of total bilateral adrenalectomy in cases of malignant hypertension.

I am aware that your editorial was not primarily concerned with cases which had progressed to the malignant phase but it is in these patients that the procedure can show such dramatic results. As you have stated, partial adrenalectomy and very occasionally total bilateral adrenalectomy have so often been combined with sympathectomy or hypotensive-drug therapy that it is difficult to assess the indications for adrenal surgery alone as opposed to other procedures You also point out that the blood pressure per se may not be influenced by adrenalectomy and for this reason I have hesitated to operate on any case with straightforward "essential hypertension. But most clinicians would agree that once papillœdema has developed the expectation of life can be measured in months not years so the patient has nothing to lose by undergoing total bilateral adrenalectomy

My experience of this operation is limited to twelve patients but the results have been most encouraging so far The five patients originally reported [1] continue to lead active useful lives, and five subsequent cases are equally encouraging The longest survivor (20 months) was probably the most acutely ill patient of the series having very severe cardiac failure with pulmonary congestion and pronounced visual disturbance

Cardiac failure with generalised œdema pulmonary congestion and severe eye changes are no contraindication to adrenalectomy, and can be dramatically relieved by the operation even if there is no change in the hypertension If the renal function is depressed the patient will die but it is difficult to define the limits of safety Both of my postoperative deaths were of pa with a urea clearance under 60% of normal

There is therefore no doubt that bila adrenalectomy can prolong life and re in cases of malignant hypertension pro are not seriously damaged If furt

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*Lancet* 1954 ii 1180
Sarkany I Birdwood G F B *Ibid* 1954 ii [illegible]

1 Hanley H G *Proc R. Soc*

made, operation must be undertaken before the renal changes are too advanced In my experience so far, renal failure, as shown by our present crude tests, can develop suddenly and progress rapidly (in one case so rapidly that within three months the opportunity for surgery had passed), and probably renal function tests should be repeated more often in hypertensive patients, in the hope of detecting an early malignant phase This is certainly more important than repeated blood-pressure estimations, since hypertension per se appears to be simply a symptom of some disease that we have yet to discover

London W 1 HOWARD G HANLEY

## NOBECUTANE AS A WOUND DRESSING

SIR,—Since the introduction of 'Nobecutane' into this country, only one report on its use has appeared, when Rob and Eastcott[1] confirmed its value following application to 200 clean surgical wounds in patients resident in hospital During recent months, over 400 dressings on both inpatients and outpatients have been carried out at the Royal Free Hospital, and it was thought that our own experiences would be worth recording

Nobecutane is an acrylic resin dissolved in a mixture of acetic esters[2] It is inflammable until dry and has no effective bactericidal power In view of results previously reported and our own, the latter does not seem to be a disadvantage

*Method of Application*—As supplied at the present time, much of the fluid may be wasted, but experiments with a spray show this to be the ideal method of application. If a spray is not available, the standard bottle cap can be modified by inserting a narrow bore tube through a hole drilled in the screw cap, and an ordinary catheter spigot used to keep it closed when not in use This modification can easily be carried out in any hospital workshop The narrow bore tube allows the fluid to be used more sparingly, and a small brush will ensure that a thin layer is applied The brush can be cleaned with acetone, which will also remove the dressing if it cannot be stripped off cleanly with ordinary dressing forceps

*Infection*—In the occasional case, slight hyperæmia of the wound edges appears on the second or third postoperative day This subsides without local or systemic effects in the course of the following 24 to 48 hours In no "clean" surgical case has wound infection developed When used on potentially infected wounds in which an abscess has subsequently developed, the elasticity of the dressing has allowed the tissues to stretch, and its transparency enables progress to be observed The film is so resilient that it must be stripped off before adequate drainage can be obtained Where post operative drainage has been required through the original incision rather than through a separate "stab," the wound has in addition been covered in the immediate vicinity of the drainage tube by a gauze and wool dressing

*Intestinal Fistulæ*—In a limited number of cases we have used the method for protecting the skin round gastric, intestinal, and pancreatic fistulæ In one really uncontrolled colostomy it was not satisfactory because the fluid contents could not be limited to a reasonable surrounding area The dressing was stripped up from the periphery and could not be made to adhere again. In all other cases skin protection was adequate

*Cosmetic Results*—Since nobecutane has vasodilator properties, accurate hæmostasis is essential, but this is an advantage to the patient, if somewhat time consuming for the surgeon A continuous skin suture is more effective in controlling oozing than a series of interrupted sutures Providing this is inserted carefully, there is little risk of necrosis of the wound edges The continuous suture is also more easily removed In many cases we have not used skin sutures obtaining accurate co aptation of the skin edges by means of interrupted subcutaneous or intradermal sutures of fine plain catgut or silk This technique is especially valuable for thyroidectomy incisions and for other operations on exposed parts of the body A thin film of nobecutane helps to maintain this apposition and yet allows unrestricted movement

*Minor Outpatient Operations*—Although thes
are of little danger to life they do throw a cons
on a busy casualty department, where dressings
being removed and replaced In these cases
also proved satisfactory, despite the extra stra
the dressing during the patient's normal work. T
pain experienced during application to an
surface is no worse than that produced by dabbi
a cut

*Advantages and Disadvantages*—These have been
by Rob and Eastcott, and our experience
findings In addition we have found that immers
for ordinary washing purposes is not precluded, a
eases the work of the nursing staff One of our
even went swimming and returned the following d
dressing intact It has been said that patients
having their wounds exposed to view This has n
experience, for the vast majority of patients
able to move about in comfort—and to compare
their fellows and to show them to their visitors.

Nobecutane is a satisfactory surgical dressi
inpatients and outpatients It is economical
saving, and it does not increase the incidence
infections Skin sutures are not always nece
improving the cosmetic results It is super
ventional dressings in those sites where these a
to apply or keep in place

I wish to thank the surgeons of the Royal Free
allowing me to use this dressing on their patient
Irene Cade, F R C S, for help in the follow up

The Royal Free Hospital
North Western Branch,
London, N W 3 A. G F

## PHILOSOPHY AND THERAPEUTI

SIR,—As a student of philosophy over m
may I comment on some of the statements
Professor Alstead in his article of Dec 25?

He asks why man is susceptible to disease whe
have been created immune to them all This is
version of the age old question "If God is all p
why did He not create the perfect man?" This
creation is hardly compatible with Professor Alstead
ment, "Most of us visualise the development
organisms through the ages as a process of gradual
Few philosophers and scientists today would d
this But the purely materialistic theory of the
which dominated the 19th century and which regard
as a mere biological accident, is becoming hard
today A number of scientists have, in our time, t
from scientific materialism to a spiritual understanding
universe more in agreement with religious belief
remarkable book *Human Destiny*, Lecomte du Nou
that science finds a purpose evident in the history
which rises above the laws of matter Since the acqu
of conscience and tradition, man can and must play
in his own destiny "Human progress therefore
du Nouy, "no longer depends only on God, but on
made by each man individually By giving man
conscience God abdicated a part of His omnipotence
of His creature and this represents the spirit of God

Disease may be regarded as one of the many h
which man has always been subjected, like death by sta
floods, marauding animals, and the more modern
of road accidents and mass warfare If he is to sur
attain to the perfect spiritual development in
with the divine plan, man must continue to rise ab
accidental environment The physician should
doubt as to the importance of his contribution to
issue by his continued fight against disease and his e
to allay human suffering wherever he finds it.

Of modern therapeutic achievements Professor
asks "If these chemical and mechanical contraptio
fact of fundamental importance in the evolvement of
destiny, why have they only now become availab
suggest that the answer is to be found in the secu
of medicine As long as medicine, science, and ph
were bound to mysticism and magic, experimentation
encouraged, in fact, it was regarded as doubting th
plan Once the scientific age was ushered in
flourished and today is the golden age of therapeutics.

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C. G Eastcott H H G *Brit med J* 1954 ii 17
[illegible], K F Olow B *Nord Med* 1953 10 302

sor Alstead rightly emphasises the importance of ng the soul of man but he is very ready to sacrifice which he regards as clumsy and erratic in contrast uman mind and its activities. He makes the challeng ement that the vehicle for the spirit of man could well have been the simple amœba rather than the gly complex organism of the mammal and he hard to believe that it would matter in the slightest way of thinking the moral and spiritual development which represents the present stage in the evolutionary would have been impossible without the development human brain through the activity of which man s y and spiritual qualities are manifest How can these qualities have been developed or made manifest at utionary level of the amœba ?

pentateuch *Back to Methuselah*, Shaw has envisaged l stage of human evolution as a disembodied spirit be disembodied implies having been embodied and the man, be it ever so frail and subject to suffering and is in my opinion the only medium through which the work of evolution can be continued and fulfilled on the l plane

low Middlesex. C BEAVEN

## EMERGENCY BED SERVICE

—Early this month the Emergency Bed Service some senior members of the medical profession the operations room to see the service at work in of stress

visitors were surprised at the amount of work in hand was suggested that it would be profitable for all hospital on officers to visit Fielden House on or before their ment and thus to acquire a more vivid impression of mo of emergency cases for which admission is required don than they could by dealing only with cases in their spitals

committee think this suggestion excellent and are lad to invite all those in the Greater London area om urgent cases are offered and who have the sibility for admission or otherwise to visit the and study its work An appointment by telephone 7181) would be a great help to those in charge

Fielden House,
ondon Bridge Street,
S.E.1

G F ABERCROMBIE
Chairman Emergency Bed Service

## CONTROL OF RATS AND MICE

—I quote from your annotation of Dec 18 on this t

lay the main strong poisons of choice are zinc phos arsenic and antu (alphanaphthylthiourea)—all after ing—but antu is unsuitable for use against *R. rattus* ford workers are properly sceptical of the value of (sodium monofluoroacetate) despite the enthusiasm hich it was first received in the U.S.A

conclusions seem to me somewhat sweeping and ertainly are not in accord with our own conclusions use of rat poisons in the Port of London where, as lt of extensive field experience and investigation sons such as barium carbonate red squill arsenious and antu have been abandoned in favour of zinc ide and, more recently the anticoagulant War and the poison sodium monofluoroacetate (popu nown as 1080) Field trials are now in progre nother water soluble rodenticide which prom further useful addition to the range of rodentic o is ample evidence in this country to prove [illegible] ices of these new rodenticides in selected op[illegible] phosphide with a variety of solid bait [illegible] in with both a variety of solid bait bases [illegible] solution and 1080 as a water solution [illegible] lid bait bases While only zinc pho[illegible] in are in general use throughout th[illegible] have been proved and have been [illegible] rt of London for several years

can be dangerous if the corre[illegible] g and adequate safety precaut[illegible] but no difficulty whatever has been experienced by trained operators working in the Port of London It has proved in their hands to be a highly valuable, efficient, and readily acceptable rodenticide capable of a decisive kill overnight By its use it is also possible to secure an appreciable saving in man hours an advantage of paramount importance in port conditions where prompt action is essential It is by the selective use of zinc phosphide warfarin and 1080 that the Port of London is kept remarkably free from rodent infestation

Guildhall London E.C.2

J GREENWOOD WILSON
Medical Officer of Health,
Port of London.

## OPERATIONS ON THE HEART

SIR,—I read with interest your leader of Dec 25 and find myself in agreement with much of what Dr Cort wrote in his letter last week

Our paper[1] was concerned only with metabolic disturbances observed after mitral valvotomy Administration of saline after operation is indicated only if the patient is sodium depleted This was occasionally observed in those with mitral stenosis who had been free of œdema but had nevertheless been treated with a low salt diet and mercurial diuretics in preparation for operation After valvotomy there is an exudate from the wound and pleural cavity of fluid rich in sodium. If the body sodium content has been considerably reduced preoperatively, and this secondary loss after operation is large and uncorrected true sodium depletion may develop In such exceptional circumstances but in them alone, hypertonic saline produces a rapid and lasting improvement in both the clinical and biochemical state of the patient

The fall in serum-sodium concentration regularly observed during the first week after operation is not usually associated with a loss of sodium from the body and is certainly not an indication for giving additional saline This fall is transient and is due at least in part to water retention I do not wish to encroach on your space to discuss the wider aspects of hyponatræmia in cardiac patients apart from operation on the heart valve and should only like to endorse Dr Cort's remarks regarding hypertonic saline In patients with persistent hyponatræmia the total body sodium content measured by isotope dilution [illegible] greatly increased in spite of the low serum concentration The administration of saline simply aggravates the condition by leading to further retention of water in excess of sodium.

Sheffield G M [illegible]

## [illegible] EPILEPSY

SIR,—I think [illegible] said [illegible] Dr W[illegible] [illegible] [illegible] in his own [illegible] from [illegible] [illegible]

[illegible]

[illegible]

ond iring rtuo- s less gists in r towns ? ough work s o too much tor the general hat the broader a senior registrar in dermatology rs : I said then cialties and as strars appointed lty of acquiring who "abdominal migraine," at least while we have no method of removing the mask, and neither response to phenobarbitone nor, as yet, electro encephalography can be said to be reliable mask removers

Rapid and easy extension to cover more and more of the phenomena of ill health has always been the danger of the unifying concept, and it is only too easy to say that bilious attacks, temper tantrums, nightmares, bedwetting, obscure recurrent pains, and many other transient disorders may be due to masked epilepsy, though it is difficult to see how this helps We can try phenobarbitone in some of these cases without making a diagnosis which is likely to continue to have distressing social implications in spite of all our reassurances

Royal Berkshire Hospital
Reading

J J KEMPTON

SIR,—I was most interested in Dr Wallis's article on "Masked Epilepsy" as I believe that the condition he describes, whatever name one gives it, is not uncommon

I note that he obtains good results from treatment with phenobarbitone, but he does not mention any toxic effects from the drug I have found that protracted administration of phenobarbitone to children frequently produces behaviour disorders and irritability, and I now always warn parents about this, and if necessary use another anticonvulsant drug such as primidone

Boxhill-on-Sea

LESLIE SCOTT

## CORTISONE AND CLOSED CRUSH INJURIES OF THE HAND

SIR,—Crushing injuries of the hands in which the palmar and digital tissues are permeated by an effusion of blood and the palmar spaces are distended rank among the most crippling of injuries Treatment is long, recovery slow and incomplete, and permanent disability common

Only two cases are here presented, but their progress was so extraordinary that the matter seems worth bringing to the notice of all who are required to treat hand injuries

CASE 1—A girl of 6 was admitted to hospital after a concrete clothes post had fallen on both her hands and crushed them on a concrete slab The hands were covered with superficial abrasions and grossly swollen The palms were ballooned and tense and the fingers immobile There was no bony damage The child was shocked and in great pain The hands were moulded as far as possible into the position of function, pressure dressings applied, and the hands elevated

Six days later the abrasions were healing, but no active movement was possible and passive movement still caused pain Cortisone acetate (12 5 mg daily in divided doses) was then given for fourteen days' On the fifth day of treatment there was no pain, and far less tension and tenderness The interphalangeal joints moved actively through a full range On one side the range in the metacarpophalangeal joints was half normal, in the other it was nil On the fourteenth day of treatment there was no pain even on squeezing the hand, and the range of movement in all joints was almost full One month later, apart from very slight thickening on the back of the left wrist, two independent examiners found no abnormality

CASE 2—A man of 40 was admitted after crushing his left hand in a machine at work There was a laceration of the left thumb, and the swollen left hand resembled a blown up rubber glove, the palm being 3 in thick from front to back—about double the thickness of the right hand. No active or passive movement was possible in the fingers Under general anæsthesia the wound was excised and sutured, it did not extend into the palmar hæmatoma The hand was moulded as near to the position of function as possible and a pressure dressing applied Seven days later cortisone acetate (25 mg four times daily) was started and was continued until the total intake was 1400 mg Dressings were removed the tenth day after injury laceration healed by first intention On the eighth cortisone there was no pain on moving the fingers The interphalangeal joints moved through a full and the metacarpophalangeal joints lacked only The hand was slightly thickened

Six weeks after injury an independent exam that there was full movement in all the joints and a grip almost equal to that of the right hand. slightly reduced sensation to pinprick over the index finger

It seems impossible to explain the aston of recovery of these injuries except through the cortisone Healing of the abrasions and was allowed to proceed for six and seven days before giving cortisone, was not delayed by the used, and no side effects were observed. seems worthy of further trial

I am indebted to Dr J E Royds for his supervising the administration of cortisone.

Ashford Hospital,
Middlesex

DENNIS

## HEAT TO THE HEART

SIR,—I have read with interest Mr Picke (Jan 15) He rightly recommends the app heat to the cardiac region to allay attacks He recommends the use of a small electric handkerchief rung out of water at a 110°F

Anything hot emits infrared irradiations much more effective method of applying heat means of an infrared lamp emitting infrared black body element The heat from such a source tive, analgesic, and antispasmodic The measure by Mr Pickerill would, of course, be useful if an is not available

Experience has taught me that infrared applied for half an hour or so over the cardiac combined with a course of general ultravi diation, will greatly lessen the incidence of attacks

Eastbourne

W ANNANDALE T

## "TAKE A COUPLE OF FAT VIPERS

SIR,—Nicholas Culpeper, Gent Student in and Astrology, in the *Pharmacopœia Londi or the London Dispensatory* (Sixth Edition, 1655 two references to the medicinal use of vipers

On p 45 under the heading of "Living-Creat writes "The Flesh of Vipers being eaten (I tak English Adder to be the true Viper, though venemous as they are in hotter countries) clear help the vices of the Nerves, resist poyson exceeding is there any better remedy under the Sun for the than the Head of the Viper that bit you, bruised to the place, and the flesh eaten, you need not dram at a time, and make it up as you shall Troches of Vipers.

Referring to Troches he continues (p 268) man may make them into what form he pleas are usually made into little flat thin Cakes, of twenty grains in weight, *plus minus* some (as of Serpents upon Troches of Vipers) upon guild them with leaf Gold, some do neither

Does the expression "Head of the Viper th take chronological precedence over "the dog"?

Mile End Hospital
London E 1

W G

SIR,—I have an old family recipe for which resembles the one described last week by but which states that the chicken must be with parsley, that pimpernel and mace be adde after the viper is cut up and added, the wh rendered to one third of its original amount chlorophyll content, rather than the viper, ac its asphrodisiac reputation

Oxted Surrey

CHRISTOPHER

## GENITO-URINARY TUBERCULOSIS

-Tuberculosis it has been said (? erroneously) t affect both the genital and the urinary systems iently in the female as in the male Published pporting this are hard to find Search of publica n genito-urinary tuberculosis is quite often inting because they do not mention female esions which may occur before or after the urinary diagnosed

uld be interesting to know the incidence of genital among the female patients in the series of 240 genito urinary tuberculosis treated by Mr Cosbie d his colleagues and described in last week s issue

tment of Pathology
Hospital for Women
London S W 3

MAGNUS HAINES

## SULPHONAMIDE SENSITIVITY

-The following case of sulphonamide sensitivity usual features

tient was a married woman of 33 with no significant eases or family history She had had no previous ible except for an attack in February 1954 of sub nd facial oedema this lasted four days and cleared i histamines. No cause for it was discovered

ug 13 1954 she went on holiday to Eastbourne of recent 'flu' and nasal catarrh she was supplied e sulphadimidine tablets, and told to take 1 g every urs. On Aug 18 she returned from Eastbourne feeling well Her temperature was 101 8°F her pulse was nd a papular bullous erythema was present on all areas, with "butterfly" distribution on the face ted areas were oedematous The eruption which l rapidly was thought to be a sulphonamide sensitivity the sulphadimidine was stopped and treatment was ith promethazine hydrochloride 25 mg three times

days later on Aug 21 she was admitted to hospital r temperature was still 101°–102°F the rash was nd she had a severe cough The differential diagnosis me was (a) sulphonamide-sensitivity rash ; (b) lupus atosus ; or (c) bullous erythema multiforme

examination of the chest and blood-count on Sept 10 mal and the Q fever cephalin flocculation test was ; the erythrocyte-sedimentation rate (E.S.R.) how s 125 mm. in one hour (Westergren) An evening (up to 100–101 F) persisted until Sept 14 On the E.S.R was 57 mm. in one hour ; and serum were 0·4 g per 100 ml

pt 20 when the E.S.R was 42 mm. in one hour and nin/globulin ratio was 1 14 the patient was discharged pital By this time the rash had disappeared but is residual staining of the lesions. Marrow films l on Oct 11 for lupus-erythematosus cells were Tests for cold agglutinins were also negative

v 2 the E.S.R had fallen to 0 mm. in one hour and the elt quite well although she complained of her hair t. A month later there was still some loss of hair slight pigmentation at the sites of the original lesions. blesome cough persisted

namide sensitivity following exposure to light n This case is of interest in view of the following

sulphonamide used (sulphadimidine) is the least ll sulphonamides, and moreover it was used here in —1 g eight hourly for five days (total 15 g )

E.S.R. was exceedingly high at the onset of the illness in one hour) and it did not return to normal until ks later

one month there was an evening pyrexia (up to hich was accompanied by a cough That in associa- the high E.S.R. and the character of the rash was spicious of lupus erythematosus ; this diagnosis was excluded by the marrow smear on Oct 11 A h may be found in acute disseminated lupus osus or erythema multiforme

hair is common after sulphonamide sensitivity ultimate prognosis is good Marked residual pigmentation at the site of the lesions often persists till three months after the onset of the illness.

My thanks are due to Dr Quentin Evans and Dr H A Treble for permission to publish this case which was under their care in the Kent and Canterbury Hospital

Faversham Kent

EDWARD D FOX

## SANATORIA

SIR —Never at any time have there been sufficient beds available for the treatment of pulmonary tuberculosis in this country The result has been that one of two policies was adopted either patients were kept in sanatoria for long periods in order that quiescence might be reached with or without surgery or patients were given shorter periods of treatment and discharged non quiescent so that other patients could be admitted In the latter case the butter as it were was spread thinly over as many slices of bread as possible The experience of institutions adopting the other alternative shows that patients can be successfully treated, given time and determination by the patient and his advisers

It is my belief that bed rest like Christianity is often said to have failed when in reality the answer is that it has seldom been tried

The present comparative plethora of beds offers us an opportunity to tackle in earnest for the first time the problem of the chronic case which has so far proved insoluble except in institutions where the interests of the individual case were paramount and the shortening of a waiting list a secondary consideration

Liverpool.

D OSBORNE HUGHES

## VENEREOLOGY AND DERMATOLOGY

SIR —It is surprising that Dr Nicol (Jan 15) criticised my letter (Jan 8) without knowing the local conditions in East Kent and that he did so with so many incorrect statements

I did not plead : I commented on the possibility and the advantages of a combined post in venereology and dermatology in that particular area. Venereology was an independent specialty long before the National Health Service became effective in 1948 ; it never has been entirely separate although that is the agreed policy There is no evidence that our administrators have considered the problem solved and their policy is still to staff the clinics with experienced consultants In America, however the *Journal of Venereal Diseases* has ceased publication and at least one famous venereologist has decided to extend his interests and style himself specialist in chronic diseases.

A dermatologist recently appointed in East Anglia replaced a venereologist but Dr Nicol does not say that the retiring venereologist was also a dermatologist and that the advertisement stated that an extension of the dermatological services was envisaged. Anyhow why did these venereologists in East Anglia and East Kent elect to transfer to bigger towns ? Perhaps it supports my view that there is not enough work to hold the interest of a venereologist in some areas.

I did not say : It is a bad thing to have too much specialisation I said there was still room for the general surgeon and the consultant physician, and that the broader view was sometimes of value I did not say a senior registrar in venereology could become competent in dermatology by working in both departments for three years : I said there were many *consultants* competent in both specialties and as Mr King and Dr Russell (Jan 1) said that registrars appointed to one of the specialties had no opportunity of acquiring specialist knowledge of the other I cited one registrar who is working in both departments there are several others My registrar will appreciate Dr Nicol s congratulation but he knows that East Kent offers insufficient scope for him in venereology

With regard to local conditions, Dr Nicol will be pleased to hear that the clinics are adequate and they are well sited at the hub of transport radiations they are probably unsurpassed for accessibility in any part of the country The only major seaport in the area is Dover and that does not have busy clinics. The liaison with other parts of the hospitals was good it still will be if the appointed consultant is domiciled locally and is thereby easily available and has the broader view, it may not be so if his enthusiasm lags from insufficient work, or if he is often away on journeys to London to augment his clinical material I think, in view of the public health and social aspects of the work, that a candidate with a primary interest in venereology is desirable for the area, especially as he will have dermatological colleagues

As I see it, Dr Nicol is not clear about the position and with this letter my previous letter (Jan 8) remains to outline conditions in East Kent I am convinced that the essential requirements for that area are, as I stated, exceptional, and that a combined appointment is needed I now plead it

Seamen's Hospitals,
London
DAVID ERSKINE

## NORADRENALINE AND ESSENTIAL HYPERTENSION

SIR,—Dr Litchfield (Nov 27) finds fault with my hypothesis that excessive secretion of noradrenaline is responsible for raising the blood-pressure in essential hypertension because

(1) Hypertension may persist after the removal of a phæochromocytoma

(2) Numerous observations by von Euler and others on the excretion of adrenaline and noradrenaline in the urine have disproved my hypothesis

(3) Barnett et al.[1] found that noradrenaline infusions and phæochromocytoma could be distinguished from essential hypertension by reduction in hand and forearm blood flow and frequently by pallor of the skin and bradycardia

I shall answer these points seriatim

(1) That hypertension may persist (usually at a lower level) after removal of a phæochromocytoma is generally accepted, and, as Dr Litchfield says, "secretions of the tumour initiate another usually irreversible hypertensive mechanism" There is, however, nothing mysterious about the nature of this mechanism, it is that of renal hypertension

Excessive amounts of noradrenaline secreted by a phæochromocytoma or an overactive adrenal medulla raise the blood pressure and, in time, bring about in a certain proportion of cases a narrowing of the renal arterioles (nephrosclerosis) Since we know from Goldblatt's work[2] that renal ischæmia is the cause of renal hypertension, it is not difficult to account for the "irreversible hypertensive mechanism" found in some cases of phæochromocytoma

(2) A high urinary excretion of pressor amines has been found consistently in phæochromocytoma and is to be expected when we consider the large amounts of these substances present in the tumour Though figures comparable to these have never been found in other forms of hypertension, there is suggestive evidence that the excretion of noradrenaline may be moderately increased in essential hypertension

In 1947 Holtz et al[3] found an excessive excretion of noradrenaline in this condition (100–200% above normal) In 1952 von Euler,[4] in a study of 500 cases of hypertension, reported that excretion of pressor amines was normal in 60% and increased in the remaining 40% In 1953 Burn[5] found that the urinary excretion of noradrenaline varied directly with the age—an interesting finding when one bears in mind that the old have higher blood-pressures than the young He also showed that in a group of moderate hypertensives (mean 170 mm Hg systolic) the excretion of pressor amines was higher than in a control group of normotensives (80 µg as compared with 71 µg)

Though this difference may not be statistically significant, it may still be important in the light of the hypothesis advanced in my paper For if the level of the blood pressure is the result of a balance between two antagonistic endocrine glands and if the blood pressure lowering substance is deficient, then normal or only slightly increased amounts of noradrenaline might cause an appreciable elevation in the blood pressure In other words, normal noradrenaline figures might a relative increase vis à-vis a deficient blood pressure substance

(3) Dr Litchfield states that Barnett and his could distinguish between phæochromocytoma and hypertension by a reduction in hand and flow The question which naturally arises is how they knew they were dealing with essential hyperten pathological evidence and Goldblatt's work we t about 75% of cases of essential hypertension are by varying degrees of renal hypertension. The majority of cases of hypertensive disease the distinct mechanisms responsible for the elevation of pressure Furthermore, it is often impossible to given case of hypertension whether the mechani is renal or not, for extreme degrees of renal fa associated with a normal blood pressure, while function may be found with hypertension of origin

What is the hand and forearm blood flow in tension, in mixed essential and renal hyperten essential hypertension ? An answer to these que knowledge of the diagnostic criteria used by the would help in assessing the validity of their evidence

Barnett et al state that "essential hyper associated with a reduction in hand blood flow" and Fierst[6] do not agree In a study of 70 hyp 90 normal subjects they found that "the ave flow was much less in hypertensive than in control

Bradycardia is not at all uncommon in essent tension Normal and rapid pulse rates, however found This is best explained by postulating the secretion of varying amounts of adrenaline. F many factors unrelated to these secretions affect rate that it would be unjustifible to draw conclu this alone

A pale sallow complexion is common in essent tension As previously reported[7] this may become thyroid treatment In my limited experience of infusion (5 cases), I found that pallor appeared at ing of the infusion and also when the rate of flow w increased. When the drip flowed steadily there no pallor, suggesting that the body was adjusting stimulus In 2 cases when the blood pressure was at about 160 mm there was no pallor In 1 of t shortly after the initial pallor had passed off there flushing of both ears, which reminded me of the of Burn on the perfused rabbit's ear First a with Dutta[8] and later with Robinson,[9] he repeatedly dilator responses to adrenaline instead of the constrictor ones

It would appear then that noradrenaline hyperten occur in the absence of bradycardia and of pallor add that by stressing these details we confer o importance they do not possess We shall soon be see the wood for the trees

Finally, a word on Dr Litchfield's commen hypothesis is based on "very indirect evide a short paper designed to stress other facts possible to deal comprehensively with the Dr. Litchfield requires All one could do w briefly to the more recent developments evidence of the distant and more recent pa summarised as follows

(1) Oliver and Schafer[10] in 1894 produced a ris blood pressure by injecting an extract of the

(2) Cannon[11] and his associates demon emotions such as fear and rage were associated w pouring of adrenaline into the blood stream.

(3) Barger and Dale[12] in 1910 pointed out that of adrenaline and the effect of sympathetic tion were not always identical. They suggested differences occurred the sympathetic med adrenaline but a closely related compound, p adrenaline Cannon gave the name sympath

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1 Barnett, A J Blackett R B, Depoorter A. E, Sanderson P H, Wilson G M *Clin Sci* 1950 9, 151
2 Goldblatt, H The Renal Origin of Hypertension Springfield, Illinois 1948
3 P Credner, K Kroneberg, G *Arch. exp Path Pharmal.* 204 228
U S *Congr int Biochim* Paris, 1952, p 39
P *Brit med J* 1953, 1 697
6 Abramson, D I Fierst, S M *Amer Heart J* 191
7 Menof, P *S Afr med J* 1950, 24 172
8 Burn, J H Dutta N K *Brit J Pharmacol.* 1
9 Burn J H, Robinson J *Ibid* 1951, 6 110
10 Oliver G Schafer E A *J Physiol* 1894, 16, 1
11 Cannon, W B Bodily Changes in Pain, Hun Rage New York 1929
12 Barger, G Dale, H H *J Physiol* 1910 41, 1

e responsible among other actions for vaso tion and elevation of the blood pressure

inter et al.[13] in 1948 succeeded in resolving noradrena its lævo and dextro isomers and made l noradrena- ilable for experimental study All investigators found raised the diastolic and systolic blood pressures tly It is widely distributed in the body (in all ic nerve-fibres, in the blood in the urine in the medulla and in chromaffin-cell tumours) It has been d as the sympathetic mediator in which Barger and d Cannon and his associates, were interested.

ould appear then from these facts and those ied in my paper that noradrenaline excess e or relative) is a likely cause of essential nsion

esburg PERICLES MENOF

## REINFORCING PLASTER OF PARIS

The use of 'Glassona' or cellulose-acetate glass the making of splints is familiar to most Its ar advantages are its rigidity, lightness imperme o water and transparency to X rays Of these ges the most striking, to my mind is its rigidity t. It is so rigid that the removal of a forearm cutting it down one side and springing it apart quite difficult Its particular disadvantage in the nt of fractures is the slow time of setting Excel of its great rigidity however can be made in forcement of plaster of paris If it is applied on f a plaster which has already set the disadvantage rolonged setting time is overcome, as it rests on ase and is not subject to distortion while drying

found glassona of great benefit in the reinforcement cas around the groin and shoulder spicas around the he basic plaster should be applied with moderately r so that at the time of crystallisation a fair amount of ven off If the glassona bandage is then applied after ner of a figure of eight around the groin or axilla it ut fairly quickly because of the heat of the underlying No artificial aid to drying is required and the danger of an electric drier is therefore eliminated The bandages are an excellent safeguard against cracking in or axilla and permit of the application of a lighter re permeable to X rays than would otherwise be

County Hospital DAVID P THOMAS

## NOTES ON TRANSFUSION

The Ministry of Health's booklet *Notes on ion* (1954) is being revised May I put in a plea lteration?

it is stated that if bottles of blood are punctured used within 24 hours they should be labelled ous for patients In those districts where no ies are supplied this causes difficulties When asked for and the bottles punctured for a direct is sometimes not used for example the may change his mind or the patient may die or efore the blood can be given In the area where f this happens and I label the punctured bottle fter 24 hours as dangerous for patients and then e blood for another patient my blood supply ll tell me that no blood will be sent unless I first ottle that has been sampled If I refuse to do ans either withholding blood from a patient ibly risking his life or else giving a bottle dangerous for patients

tastrophe occurred and it transpired that the l been punctured more than 24 hours before ight be infected) the pathologist would be open and perhaps to heavy damages

be argued that the statement in the booklet is d not an instruction or a directive The imprimatur title and wording suggest a directive but even if it is simple advice, when handled by a lawyer in court, it would carry great weight so it becomes tantamount to a directive

May I suggest that the Ministry bring in a non separable pilot tube as a standard fitting but until then surely in common sense and common justice the advice in the booklet should be altered

CLINICAL PATHOLOGIST

## CORTICOTROPHIN AND SPLENECTOMY IN ACQUIRED HÆMOLYTIC ANÆMIA

SIR,—It has been stated that if three or at the most four blood transfusions do not control idiopathic acquired hæmolytic anæmia splenectomy should be performed[1] While some cases fail to respond to combined splenectomy and transfusion alone[2,3] a number of authors have reported encouraging results from corticotrophin (A C T H ) or cortisone treatment[4,5] Unfortunately not all patients have benefited significantly from hormones[5,6] while in some cases an initial satisfactory response could be sustained only by continuing corticotrophin or cortisone[7] The toxic effects of these drugs may however make it impossible to continue treatment[4] and prolonged therapy followed by splenectomy may result in unsatisfactory wound healing and burst abdomen moreover a second course of hormones may be less effective than the first[5] We therefore concluded that those patients who had not improved with blood transfusion might be treated most successfully by splenectomy performed during the first course of corticotrophin We have so far treated 3 patients in this way

A male clerk aged 17 a schoolgirl aged 9 and a housewife aged 29 all presented with typical clinical and laboratory findings including pyrexia tachycardia jaundice severe anæmia, splenomegaly peripheral reticulocytosis and spherocytosis, increased red-cell fragility a positive direct Coombs test normoblastic hyperplasia of the bone marrow and increased fæcal urobilinogen excretion No abnormal hæmolysins were detected but the clerk's serum contained an auto and a pan agglutinin active at 4 C and an auto agglutinin active at 20 C in saline There was also a trace of auto agglutinin active in albumin at 4 C only The schoolgirl's serum contained auto and pan agglutinins active in saline and albumin at 4 C and a trace of pan agglutinin active in saline and albumin at 18 C The housewife's serum contained auto- and pan agglutinins active at 4 C 20 C, and 37 C in both saline and albumin

As repeated blood transfusions failed to induce a satisfactory remission in any of them corticotrophin (25 mg intramuscularly every six hours) was given for eight days in the first case and for ten days in the third case prior to splenectomy 15 mg of the hormone was given intramuscularly every six hours to the schoolgirl for five days before splenectomy Gradually diminishing doses were given after the operation for six four and ten days respectively The housewife had postoperative right basal pneumonia which responded to treatment including antibiotics This incident was followed by mesenteric thrombosis from which she recovered when treated with heparin and ethyl biscoumacetate ('Tromexan') The other two patients gave rise to no anxiety after the operation

The three patients have remained well and have led normal lives for twenty four fifteen and twenty three months respectively in spite of a positive Coombs test serum auto agglutinins and spherocytosis which persist The pan

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M L Tullar B F Luduena F P *Science* 1948

[1] Dameshek, W Schwartz, S O *Medicine Baltimore* 1940 19 231

[2] Dameshek, W *Clinics* 1943 2 118

[3] Millichap J G *Arch. Dis Child* 19[illegible] 27 [illegible]

[4] Gardner F H, McElfresh A E, Harris J W, Diamond L K *J Lab clin Med* 1951 37 444

[5] Davidson L S P, Girdwood R H, Swan H T *Brit med J* 19[illegible] ii, 1059

[6] Preliminary Report to the M.R.C. by the Panel on the Hæmatological Applications of A C T H and Cortisone *Ibid* 19[illegible] i [illegible]

Sacks M S, Workman J B, Jahn E F *J Amer med Ass* 195[illegible] 150 155[illegible]

[6] Altman J D *Brit med J* 1953 i 7[illegible]

agglutinins are not detectable in the first two cases, but persist in saline and albumin at 4°C and 18°C in the housewife

We thank Prof E J Wayne for valuable help and criticism throughout, Mr W J Lytle, Mr Clifford Jones, and Mrs E P Kempsey for their excellent surgical coöperation, and Dr C C Bowley and Mr F I N Dunsford, of the Regional Blood Transfusion Centre, Sheffield, for some of the serological findings

Boston Group of Hospitals, Boston, Lincs — W J G BARRIE
Royal Infirmary, Sheffield — E K BLACKBURN

## ISOBEL CRIPPS CENTRE

Dr RICHARD MEYER writes

Dr Barlow's assumption, in his letter last week, that this centre ignores research is incorrect Mr Neil has given me facilities to take full psychiatric histories from some of his pupils before treatment, and to follow up these people after treatment He has had the courage to take on pupils who have not responded to orthodox psychiatric or physiotherapeutic treatment I feel that his method deserves our critical coöperation, rather than destructive condescension

Mr CHARLES A NEIL writes

I wish to correct the faulty impressions given in Dr Barlow's letter

I am not teaching the Alexander technique, for although I trained with Alexander between 1932 and 1937 and owe a great deal to him and will always be grateful for what he has taught me, my methods, as a result of study of methods other than Alexander's both here and on the Continent, have undergone considerable change since 1937, and differ both in detail of theory and in technique from Alexander's

With regard to safeguards, this centre has a fully qualified medical adviser, who examines all the people who come here who are ill or suspected of illness and who are not already under medical care I do not "deal" with such conditions as asthma in the sense that Dr Barlow implies, but confine myself solely to teaching the pupil to manage his body better, and this with the approval of the pupil's doctor

# Public Health

## Maternity and Child Welfare in Glasgow

Dr Stuart Laidlaw, medical officer of health for Glasgow, reports [1] that in 1953 the infant-mortality rate (36 per 1000) was the lowest yet recorded in that city As in other parts of the country, the decline in the rate over recent years is accounted for mainly by a reduction in the number of deaths after the first month of life, stillbirths and neonatal deaths show no corresponding decrease, yet many of these, Dr Laidlaw remarks, could be prevented by better obstetric care and better education of the expectant mother Consequently he regrets that attendances at antenatal clinics once again fell Every effort was made to secure the coöperation of the general practitioners in advising expectant mothers to attend mothercraft classes and special consultant sessions at the clinics, but the response was very poor Thus, of 2479 expectant mothers who attended these sessions, only 150 were referred by their family doctors

Drawing attention to the continued need for educative work by the maternity and child welfare services, Dr Laidlaw reports that of the 58 violent deaths of infants under 1 year of age, more than half were from asphyxia following inhalation of vomit or regurgitation of food, and 23 were from suffocation by pillows, bed covers, or over laying Among children aged 1–5 accidents and violence accounted for more deaths than any other cause, accidents in the home were responsible for 7 of the 21 deaths in this group, and road accidents for another 7

Regarding mental hygiene, Dr Laidlaw reports that in Glasgow more attention is being paid to the preventive aspect of child psychiatry A special "problems clinic" has been established, at which parents are helped to resolve tensions in the child's environment and to strengthen the child to cope with difficulties which cannot be removed Cases in which definite breakdown has occurred are recognised in the clinic and  
the larger child-guidance centres. During  
patients attended the clinic, and in 32 a  
solution was reached

During 1953 the B C G vaccination camp  
extended to school-children aged 13 years.  
consent to vaccination was granted in 11,59  
11,206 children proved Mantoux-negative,  
of these received B C G vaccine In recognit  
successful campaign, the National Baby Welfar  
has awarded the William Hardy shield to Gl  
most meritorious performance in children's we  
1953

## Tuberculosis Waiting-lists in

Until 1954 the number of tuberculous  
awaiting admission to Scottish hospitals had  
fallen below 1600, between March and Septem  
year, however, the numbers fell abruptly  
to 841 This decline cannot be entirely attr  
decrease in the prevalence of the disease  
on the figures, Dr I M Macgregor,[1] of  
department of health, observes that in nearly  
"there has been no evidence of a comparable  
in the frequency of new notifications." In  
months of 1954 the number of notifications in  
and Lanarkshire was in fact 15–17% greater  
equivalent period of 1953, and even in C  
the waiting-lists show the sharpest decline,  
decreased by only 7% Assessing the  
reduction in the waiting-list, Dr Macgreg

> "More patients are now under active medical  
> their own homes supplemented by periodic visits  
> clinic Waiting lists have been purged and  
> reduced by the removal of those no longer in  
> care Although national statistics are not  
> evidence that a combination of hospital and home  
> is materially reducing the length of institutional  
> can be no doubt that recent advances in medical  
> earlier case recognition and improved housing  
> an increasing number of the tuberculous within  
> effective cure without hospitalisation"

## Smallpox in France

The French ministry of public health and  
in a message dated Jan 8, reports that the  
25 cases of smallpox in the Vannes area, with

The 1st case occurred at the beginning of D  
unvaccinated child aged 1 year The child's  
returned 10 days previously from Indo China,  
been in a hospital in which cases of smallpox  
treated All persons resident in the Vannes area  
vaccinated

A press report from Paris, dated Jan. 12,  
total number of cases as 40, including 4 dea  
departments in Brittany, the largest number  
the Morbihan department

## Statistics for England and Wales

The Registrar-General has announced [2]  
figures for the third quarter of 1954 Births  
to 15 0 per 1000 population, as against 15·6  
the corresponding quarter of 1953 The stillbir  
22 9 per 1000 total births—was 1 9 higher th  
third quarter of 1953 The death-rate was 9  
population, compared with 8 9 in the third  
1953 The infant-mortality rate—21 per 10  
live births—was the lowest yet recorded for an

The home population of England and Wales is  
to have been 44,274,000 on June 30, 1954, this is a  
of 500,000 since the last census (April 8, 1951) In  
ended June 30, 1954, persons aged 65 and over are  
to have increased by 108,000, and children aged 0–14  
persons aged 15–64 decreased in number by 20,00

In the second quarter of 1954, deaths from  
tuberculosis (1657) were 9% fewer than in the  
quarter of 1953, and deaths from cancer (21,826)  
275 more than in that quarter

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of the Medical Officer of Health City of Glasgow, 1953

[1] Macgregor I. M *Hlth Bull*, *Edinb* 1955, 13 4  
[2] Registrar General's Return for England and Wal  
quarter ended Sept 30, 1954 H.M. Stationery Off  
2s

# Obituary

## HAROLD WORDSWORTH BARBER

M.A., M B Camb F R C.P

H W Barber who died in London on Jan. 14 age of 68 was the first physician to be appointed staff of Guy's Hospital as a specialist in dermatology no other duties

was born in Nottingham the son of a solicitor; o was educated at nearby Repton from which he scholarship to Clare College Cambridge. In 1908 k a first class in the natural sciences tripos and years later he qualified from Guy's Hospital In he was awarded the Arthur Durham travelling ship He had by then determined on a career in dermatology, and most of his year's tenure was spent in Paris; but he also studied under Unna in Hamburg He returned to Guy's as medical registrar He was also appointed dermatologist to the Evelina Hospital and in 1915 to the Prince of Wales's Hospital Tottenham. In that year he joined the R.A.M.C and he served in India Mesopotamia, German East Africa, and France After demobilisation in 1919 he resumed the medical registrarship at Guy's, and soon afterwards he was appointed dermatologist to the hospital In 1922 he was elected F.R.C.P He served as president of the British Associ of Dermatology and of the dermatological section Royal Society of Medicine and he was consulting tologist to the Royal Navy

Elliott & Fry

his Lettsomian lectures to the Medical Society of n in 1929[1] Barber made a compelling plea for tegration of dermatology with general medicine r more extensive training of the student in this t Of the student's training he said

> it is but logical that he should be first taught to see orpret what he sees, and it is in imparting this faculty rvation and deduction that the dermatologist should chief métier in the early stages of a student's training"

e concluded:

> ignorance of the most elementary principles of the logy and pathology of the skin is it must be admitted read among our profession I believe this to be due to the fact that dermatology has been practically l in the qualifying examination and partly to faulty g of the real significance of cutaneous disorders and ns in relation to general medicine

breadth of his view is partly explained in the ing tribute from G B D:

om inclination as well as upon the advice of Cooper Harold Barber chose to study dermatology spending eater part of his year abroad in Paris under Darier hom thereafter he maintained a lifelong friendship department at Guy's he followed a line of great figures dicine in the latter half of the 19th and the early 20th ies—Addison Gull Samuel Wilks, Pye Smith and Perry Like his illustrious predecessors he possessed oundly interesting mind and for a long while he may be said to have dominated thought in British derma

He was hardly ever content to accept morphology end of knowledge even for the moment though he obably as well equipped with knowledge of that aspect matology as anyone living He communicated his ations and ideas in a large number of papers written eccable style always interesting and arresting some leaving the reader with the impression that the aries of pure reasoning had been perhaps a little pped but always providing food for thought

rber was a romantic and this was reflected in the o of his home and possessions and the beauty of his garden which he tended himself He found and enjoyed beauty everywhere in nature including human nature At the time that I knew him best he also enjoyed the simplest forms of recreation deriving almost boyish pleasure from fiction of the more exciting type from watching cricket and from following the fortunes of his often disappointing County even the bustle of a big railway terminus and a journey on a fast train gave him pleasure

With the qualities that he possessed of great erudition and enthusiasm and outstanding personal attractiveness, it was natural that he should attract to himself a large body of students of all ages who were convinced that there was no-one like Barber and never would be Inevitably the same qualities brought him an overwhelmingly large practice with its attendant responsibilities and stresses. Barber worked far too hard all his life but there is no doubt that he could like Kipling's famous tramp say at the end

So write before I die he liked it all.

Dr Barber married Juliette Louise daughter of Mme Veuve Champrenaud of Paris. There were no children of the marriage

## GLEB von ANREP

M A. Camb M D Petrograd D.Sc. Lond., F R.S

Dr Gleb von Anrep who had held the chair of physiology in Fuad I University since 1931 died in Cairo on Jan 9 at the age of 63

Though of Swedish extraction he was a typical Slav He was born in St Petersburg—practically in a laboratory for his father, Prof Basil von Anrep who discovered the local anaesthetic action of cocaine lived over his place of work. He studied medicine at the Medical Academy in St Petersburg and was still a student when he embarked on his research on conditioned reflexes.

He first visited this country in 1912 when Pavlov sent him to demonstrate to Starling the effects of vagus section on pancreatic secretion and in return to learn the technique of the preparation of secretin At the end of that year he produced his first paper in the *Journal of Physiology* in which he showed that stimulation of the splanchnic nerves liberated adrenaline from the suprarenal glands which contributed to the resulting rise in blood pressure In the following year he joined the Physiological Society

That summer he again visited London to work at University College and in 1914 he brought Babkin with him. They both returned to Russia on the outbreak of war in August. Anrep who had qualified that year served as a medical officer with the Imperial Army until Russia withdrew from the war in 1917 On his return to Petrograd he lectured for a time at the Institute of Experimental Medicine and took his M.D degree In 1918 he joined the forces of General Denikin On their defeat he made his way to England and in 1920 he was appointed an assistant in the department of physiology at University College He continued his studies and obtained the degrees of M.Sc and D.Sc of the University of London. In 1925 he was naturalised and his father joined him to live in London.

In 1920 Anrep moved to Cambridge, where he was offered a lectureship and two years later he was elected F.R.S Other academic distinctions which he received in this country before he left for Egypt in 1931 included the Sharpey-Schafer prize the William Mickle prize the Sydney Ringer lectureship, and the fellowship of University College He was also appointed to a Co Lane lectureship at Stanford University California

C L F writes: Anrep was a most attract dynamic personality—an entertaining racon lecturer, with a wide knowledge of physio elegant if temperamental experimenter capacity for work. He was a fine linguis Arabic well. During his time in Cair expert and intrepid desert explorer He Starling was only exceeded by his first master Pavlov The account reflexes which he wrote for *Rec* in 1925 was the first account of in English but he knew the the subject so intimately that in a very short time.

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[1] *Lancet* 1929 ii 363 483 591

## GEORGE HALL

### C M G , M D Lond , B Sc Durh , F R C P , J P

Dr George Hall, formerly physician to the Royal Victoria Infirmary, Newcastle upon Tyne, died in that city on Jan 10, at the age of 76, after a long illness

He was born at Bishop Auckland, co Durham, where he received his schooling He had a distinguished academic career, graduating B SC from Armstrong (now King's) College, Newcastle, and then proceeding to his medical studies at University College, London There he won the Bucknill entrance scholarship, the Cluff prize for anatomy, physiology, and chemistry, the gold medal and exhibition in physiology, and later the Atkinson Morley surgical scholarship He obtained the London M B in 1903, the M.D in 1905, and the M.R C P in 1907 At University College Hospital he was house-physician to Dr Sidney Martin, house-surgeon to Mr Arthur Barker, and for nine months clinical assistant to Sir Thomas Barlow He then became junior house-physician at the National Hospital, Queen Square, and after twelve months senior house-physician. From this post he resigned after six months to begin consulting practice in Newcastle, and in 1908 he was appointed assistant physician to the Royal Victoria Infirmary In 1911 he was elected a fellow of University College, London

King's College, Newcastle

When war came in 1914 he was mobilised with the 1st Northern General Hospital, T A., but he left in 1915 to join the Egyptian Expeditionary Force as officer in charge of the medical division, 17 General Hospital, Alexandria For his services there he was appointed C.M G and was mentioned in despatches During 1916–17 he was officer commanding the Military Infectious Diseases Hospital, Choubra, Cairo , and in 1918 he commanded the 59th General Hospital, British Expeditionary Force, France

On his return to Newcastle he resumed the active life of a teaching-hospital physician together with consultant practice, chiefly in neurology During the twenty years that he was assistant physician at the Royal Victoria Infirmary, his chief was Dr Thomas Beattie In 1927 he was appointed physician, and in the same year he was elected a fellow of the Royal College of Physicians His interests were mainly neurological, and he was consultant neurologist to the Sanderson Orthopædic Hospital for Children He was also physician to the Ingham Infirmary, South Shields, and to the Ministry of Pensions Hospital at Dunston Hill He wrote a number of papers on general medical and neurological subjects, including one of considerable interest and importance on neuropathic keratitis He retained a warm affection for London and for University College, and examined for London University and the Conjoint Board

F J N , to whom we are indebted for some of the details, adds

" Hall was a handsome man, of quiet voice, modest but sociable equable in temperament, he was greatly liked by colleagues and students He was meticulous in the discharge of his duties gentlemanly, and cultured He loved music and helped in the organisation of the Newcastle Chamber Music Society He played a good game of golf His latter years were made lonely by the death of his wife in 1949 and by the inevitable departure from home of his son and daughter "

P H M -B first met George Hall in Egypt during the first world war

" He had that sweetness of nature, that coöperative forthcomingness which renders personal relations pleasant yet he tempered his associations with shrewdness and judgment of character I can never forget the kindness and consideration he showed as my O C at the Military Hospital at Choubra, and his counsel and help when I was endeavouring blish a clinical laboratory service This was his first with dysentery, malaria and many other exotic but he soon mastered the essentials and accorded this service first-rank importance As a successful administrator, his steady and calming influence radiated through the medical and nursing staffs, and indeed a happy ship His knowledge of medicine was and he was well versed in modern methods of but in the art of handling patients he was supreme "

F M R W *says of him*

" The death of George Hall ends a friendship of years' standing, dating from the days when we together in Egypt during the first world war I learnt to admire his clinical competence, his respect for his his wry but philosophical acceptance of the burdens of hospital administration which became his when he was charge of an infectious diseases hospital, and his integrity

" Separated by the distance between Newcastle and from those days onwards, we met comparatively seldom to meet him was always a refreshment We enjoyed our preliminary grumbles about the way things shaping in medicine and exchanged again our recollections of how much better everyone and everything when we were younger All this, of course, is one legitimate satisfactions of the elderly, is no more than the prides and visions of youth, and is compat the quiet enjoyment of life that was Hall's until the of his wife, a blow from which his spirit never recovered

" He was always a sound and conscientious physician a most unselfish and modest man, and to enjoy his was a privilege "

C E K , who became acquainted with Hall end of his career, recalls his especial affection for trained in his old hospital and his pleasure in his to a fellowship at University College

" He was not self seeking but a most kind, generous constant friend He was a modest person and his real as a man and as a physician was not immediately though in the course of time one became more and conscious of it, so that those who esteemed him most those who had known him longest His best friends old friends and I doubt whether he had any enemies "

# Appointments

**South East Metropolitan Regional Hospital Board**

ADCOCK, F A., M R C.S D M R.D asst radiologist Bromley
AZZOPARDI P G M D Malta, F F.A R.C.S D.A anæsthetist, Medway and Gravesend group
BELL, G J M B Lond , D P M consultant psychiatrist physician-superintendent, Darenth and Stone group
BELL, I G D M B Durh D M R T consultant in radiology Medway and Gravesend group
BOYD C H M B Leeds D A consultant anæsthetist, group
DAVIES D G H M R C S , D.A. consultant Greenwich and Deptford group
EVANS G M M D Lond., M R.C O G consultant and gynæcologist Bromley group
GLOVER J A , M D Camb , M R C P consultant south-east Kent group
GOULD J H M B Lond. M R C P , D.P M consultant trist St Francis and Lady Chichester group
HAFNER, R H V , F R C.S consultant orthopædic Medway and Gravesend group
HART, M F , M.D Lond., M.R C P consultant in medicine Bromley group
HUBAND E , M L L P.M. consultant psychiatrist, child-guidance clinic
JONES J S , M B Lond asst chest physician, south- and Isle of Thanet groups
KATARIA M S M.R C S D I H D P H asst (geriatrics), Camberwell group
KEAT F C B S , M C , M.D Lond M R.C P consultant ician Brighton and Lewes and mid Sussex groups
KING M B M D Lond consultant pathologist Kent group
NEWSTEAD SHEILA M. M B Lond M.R.C P asst. Orpington and Sevenoaks and Bromley groups
PHILPS, F R. M B E M.D Lond D I H consultant Eastbourne and Hailsham group
SANDFORD, F M. M R.C.S , D.A. consultant anæsthetist group
SAUNDERS K. E , M D Lond asst clinical pathologist group
SZUMOWSKI PIOTR M D Cracow clinician in (S H M.O ) Isle of Thanet group
TEES, J E M R.C.S , F F.A R.C.S D.A consultant Medway and Gravesend group
TUFFILL, S G , M B Lond , F.R.C.S consultant surgeon Lewisham group
VAN DORP CAROLINA M. F R C.S D.L.O consultant surgeon Camberwell group
WHEELER, P H M B Camb M R C.P D.P.M psychiatrist and deputy physician superintendent St and Lady Chichester group
ZAUSMER D M., M B Lond , D P M. asst psychiatrist child-guidance clinic

# Notes and News

## DENTIFICATION OF NEWBORN INFANTS

esfield and District Hospital Management Committee vestigate a method of recording the identity of new fants which it is said reduces to a minimum the risk s.[1] Under the proposed system which is practised United States separate bracelets bearing the birth o fastened to the wrists of the mother and her baby they leave the labour ward these bracelets can be d only by the hospital staff Until this arrangement made all infants are to be identified in the usual way labour wards, and their sex confirmed and recorded ct day by a senior midwife Printed identity cards the cots are to replace the strips of adhesive plaster y used; and the terms boy and girl are to be the maternity staffs instead of male and female committee s recommendations follow a recent incident h the sex of a baby was recorded erroneously by a both in her ward report book and on the notification

## CLINICS FOR SPASTIC CHILDREN

experimental outpatient centre for diagnosing and g cerebral palsy in children under five is to be opened ate spring at Cheyne Hospital for Children 61 Cheyne London S W 3 The centre founded by voluntary ons will be administered by Chelsea Hospital Manage ommittee

ew centre for spastic children was opened by Lady on Jan. 5 at Heaton Moor Clinic Stockport Cheshire nic, which has been established through the efforts of tional Spastics Society provides physiotherapy speech y and other facilities for fourteen local spastic children tional therapy will shortly be introduced for older n

## BRITISH STANDARD OR ERYTHROCYTE-SEDIMENTATION TUBES

ew British standard (B.S 2554 : 1954) specifies dimen finish, and length and numbering of graduation marks es for estimating the erythrocyte-sedimentation rate estergren s method by Wintrobe s *method and by a* method Copies of the standard (2s 6d ) are obtainable he British Standards Institution Sales Branch 2 Park London, W 1

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## rsity of St Andrews

ecent examinations the following were successful

—Avril Oatway (*with commendation*), B O Igwebe
*Ch.B*—Sheila E. Cheong J S Cook, J L Crichton Dattner P A. E. Edmundson J G McDonald, Anne M llvray A. J Mackenzie J A C. Macmillan, Yvonne D . A. R. Taylor Anne M Thomson Sheila K. Tod T H E. .

## rsity of Glasgow

Jan. 15 the following degrees were conferred :

—Alick Isaacs A. W Sloan (*honours*); Robin Murdoch *commendation*) R G MacFarlane Jessie L. Sharp (*com tion*) R D H Maxwell R. W Simpson
*Ch B.*—G R. MacG Barr R. D K. Buchan P R Derbley Graham, W H Hunter J F Hyslop E N Icleke, R. W lum, T N McComb R. D McDougall, M. J McFadden Macfarlane, W M. Macfarlane Ian McGregor I R. MacLaren McLauchlan Laurence Monaghan Parsooramen Paratian Robertson Hugh Sutherland Margaret A F Thom.
In absentia

## national Pharmaceutical Congress

general *assembly of the Fédération* Internationale maceutique is to be held this year in London from 19 to 23 under the presidency of Sir Hugh Linstead er particulars may be had from Mr D F Lewis F.P.S., loomsbury Square W C.1

## ish Health Services Council

eight new members appointed to this council until 31 1957 include Dr J T Baldwin general practitioner uk Dr Catherine Harrower O.B.E general practi r Glasgow Dr S I A Laidlaw, medical officer of Glasgow and Dr Douglas Miller obstetrician Royal mary Edinburgh Dr P K McCowan and Prof G M art are among those reappointed until Dec 31 1957

## Royal College of Surgeons of England

At a meeting of the council on Jan. 13 with Sir Harry Platt the president in the chair a Moynihan lectureship was awarded to Prof H. Olivecrona of Stockholm. Dr G U Cunningham, senior lecturer in morbid anatomy and histology at St Bartholomew s Hospital, was appointed Sir William Collins professor of human and comparative pathology in the college and Dr John Vane was appointed senior lecturer in the department of pharmacology

Diplomas of fellowship of the faculty of anaesthetists were granted to S M Wilson and A. H. Kasasian The following diplomas were granted jointly with the Royal College of Physicians :

*D O*—C Chowdhary
*D.M R T.*—J W Logan
*D C.H*—J A Fay
*D.A*—Catherine K Adam R. D Allan H B Aronson, A C Ashton, L. M. V Attygalle I S Barclay K. W Baruch Kenneth Bliss J A. Blundell, Janet C Bra b June E. Brett H D Browne Mavis Buck, Fodla B K Burnell, Anthea M. Bushby I R. Chalk Peggy J Clark Roberts Sheila R. Clarke J A Clover I McI Cochran A R. Cohen Phyllis Connor, C M. Conway H M C Corfield L. G B Cumpston P N Cunliffe Muriel D Dalby Margaret C D Daniel, W R. Daniel, E. J D Arcy John Davenport J W Desmond J D Dickson, Maria T D Coon Asensi B O Dowdell H D Doyle Winifred B Drew Beatrice M. Evans Rosemary A Faull Leo Feldman, Peter Flinton H G Francis J E S Gould, Elizabeth Green Joseph Greenan N R. Gupta, S J Halkett, I M Hallack G G Harrison H I Heffernan, R. S T Hey J D Holdsworth, Thelma B Hoyh Elaine V Hulse, Molly C Jacklin, J R E Jenkins E. G R. Jones Kevin Kennedy A R. Kerr Alexander Kilpatrick, D W King Michael Lauchlan Lucy T Lee, Heather J Lopert Dorothy J Lucas G F Lynam, Ian Macphail Eunice D Martin Prabhakar Mayabhai Mehta Catherine H M K Mellen, Maung J R. Millar William More B D Morison Annie Mortell, S. M MacD O'Brien Moran Helen B O Hea R H Oram, Budding Phillips A P Poole, Freda F Prince White T C Probyn Kalwar Raghavendrarao Rama Rao Stella J E Randall Mullapudi Venkata Rao J T Russell Yvonne K. Russell Dilip Kumar Sen Margaret H N Smith, Basil Solomon Jean P Spalding Henry Stabile H W Stanley Alan Thorogood J N Thorpe Francois Turrettini, C. H. van Hasselt, I R Verner N A Vincent Betty R. Waltier A N L. Watt, R. P Wise W S Wren T M Young
*D L.O*—S E M. Bates, Chhedi Chowdhary, Abdul Rasul Noormill Dhanji D A T Farrar G F Fennell, A N Griffith G M. Homan, Bhabanand Jha, Mohammed Sadiq Khan Pramod Mansukhlal Kothary Mangat Varughese Kurian J T Lees N G McGuire J A M. Martin J R Purvis Derek Russell, J R. Samuel, Sat Dev Sethi Thommandram Muthuswamy Srinivasan, Maung Maung Wain, Wijetunga Mudiyanselage Karunatilake Wijetunga

On Monday Feb 14 at 4 P.M at the college Lincoln s Inn Fields London, W.C.2 Sir Cecil Wakeley will deliver the Hunterian oration on Hunter and Surgical Research

## Postgraduate Lectures in Psychiatry and Child Guidance

A course of lectures on these subjects will be given at the St Marylebone Hospital for Psychiatry and Child Guidance 48 Conway Street Marylebone Road London N W 1 on Wednesdays at 5 30 P.M Dr Doris Odlum will give the *first lecture on Feb 2 on the relationship of psychiatry to* general medicine Other speakers will include Dr Colin Edwards, Dr R D Newton Dr Michael Fordham, Dr E. H Larkin, Dr E A Bennet Mr G C Knight Dr J Loewenstein Dr J Flind Dr F D Wrede Dr A. McClashan and Dr Colman Kenton The lectures are open without fee to doctors and senior medical students

## Chronic Rheumatic Diseases

A course on this subject *including lectures* ward rounds, and practical demonstrations, is to be held at the rheumatism unit of St Stephen s Hospital Fulham Road London S W 10 on Saturday and Sunday March 19 and 20 under the chair manship of Sir Adolphe Abrahams Prof Leslie Banks will give the opening lecture on Social and Economic Aspects of the Rheumatic Diseases Other speakers will include: Dr Francis Bach Dr Grace Batten Dr Raymond Daley Dr Philip Ellman Mr H F Harding Dr F Dudley Hart Dr J A Purser Dr P D Sanman Dr Frank Sargent and Dr Gordon Signy Further particulars can be had from the Secretary Fellowship of Postgraduate Medicine 1 Wimpole Street W 1

## International Embryological Conference

The annual meeting in Brussels, of the editorial board of the *Journal of Embryology and Experimental Morphology* is to be accompanied by public scientific sessions on April 4 All interested scientists are invited to attend and to participate in the discussions on the papers read. Those travelling from the United Kingdom should communicate with Mr D R Newth, PH.D Department of Zoology University College London W C 1 ; others should inform Prof A M Dalcq 97 rue aux Laines Brussels

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[1] *Macclesfield Times* Dec 16 1954

## Royal Edinburgh Hospital for Nervous and Mental Disorders

Dr T A Munro, physician in psychological medicine to Guy's Hospital and physician to the Royal Bethlem and Maudsley Hospital, was appointed in November, 1954, to succeed Sir David Henderson as physician superintendent to the Royal Edinburgh Hospital for Nervous and Mental Disorders

Dr. Munro was educated at Edinburgh Academy and Edinburgh University and also at Harvard and Johns Hopkins Universities After a period on the staff of the Edinburgh Royal Hospital he was appointed to a Beit memorial research fellowship and worked for some years with Prof L S Penrose, F R S in the research department of the Royal Eastern Counties Institution at Colchester He has published papers on the rôle of recessive genetic factors in the production of mental disorder and of phenylketonuria During the war years he was at first in whole time charge of a neurosis centre in County Durham in the Emergency Medical Service Later he was a specialist psychiatrist in the Army at home and overseas During the last victorious campaign of the 14th Army he was consulting psychiatrist to the Allied Land Forces in South East Asia with the rank of brigadier, later being transferred to India as consulting psychiatrist to the Army in India In early 1947 he was appointed physician in psychological medicine to Guy's Hospital

## National Association for the Prevention of Tuberculosis

The Fourth Commonwealth Health and Tuberculosis Conference of this association will be held at the Royal Festival Hall, London, from June 21 to 24 The speakers will include Sister Mary Aquinas, Dr P V Benjamin, Dr M G Constantinides, Dr George Day, Dr Johannes Holm, Dr W P D Logan, Dr E L Ross, Prof Andrew Semple, Dr Honor Smith, Dr Harold Trimble, and Prof Arvid Wallgren Further details may be had from the secretary general of the association, Tavistock House North, Tavistock Square, W C 1

## International Hospital Congress

The mental well being of patients in the general hospital is to be the main theme of the congress which the International Hospital Federation is to hold in Lucerne, Switzerland, from May 29 to June 3 Further particulars may be had from Captain J E Stone, hon secretary and treasurer of the federation, 10, Old Jewry, London, E C 2

## Laboratory Animals' Bureau Congress

Sir Howard Florey, F R S, will open this congress, which is to be held at Oxford on March 28 and 29 Other speakers will include Prof J H Burn, F.R S, and Prof B S Platt Further particulars may be had from the bureau, M R C Laboratories, Holly Hill, Hampstead, London, N W 3

## International Congress for Speech Therapy

This congress is to be held in Barcelona from Sept 3 to 7, 1956 Further particulars may be had from Dr J Perelló, Provenza 319, Barcelona, 9, Spain

## Hunterian Society

The annual dinner of this society will be held at the Savoy Hotel, Strand, London, W C 2, on Thursday, Feb 10 Tickets (31*s* 6*d*) may be had from Mr R S Murley, 95, Harley Street, W 1

## Higher Rates of Insurance Benefits and Pensions

The dates from which the increased pensions and other National Insurance and Industrial Injuries benefits, provided by the National Insurance Act, 1954 (see *Lancet*, 1954, ii, 1236) will be paid have now been fixed as follows

April 25 for retirement pensions widows benefits, guardians' allowance and industrial death benefits
May 16 for maternity benefits
May 19 for unemployment benefit, sickness benefit and industrial injury and disablement benefits

The higher National Insurance and Industrial Injuries contribution rates will be introduced on June 6

Hospital inpatients, after certain periods of free treatment, receive benefits at reduced rates These reduced rates are to be increased For example, after eight weeks in hospital the benefit of patients with dependants will be reduced by 7*s* 6*d* a week, normally leaving the married couple with 57*s* 6*d* a week (instead of 47*s* 6*d* after the present reduction of 6*s* 6*d*)

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A memorial service for Sir Alfred Howitt will be held at the Chapel of St Thomas's Hospital, London, S E 1, at 12 15 P M Jan 27

# Diary of the Week

JAN 23 TO 29

### Monday, 24th

MANCHESTER MEDICAL SOCIETY
9 P M (Medical School) *General Practice* Dr Robert
Recent Advances?

### Tuesday, 25th

UNIVERSITY COLLEGE, Gower Street, W C 1
5 30 P.M Prof J Z Young, F R.S Language of
its Advantages and Limitations
BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P M (London School of Hygiene and Tropical
Keppel Street, W C 1) Dr Janet Vaughan
Effects on Bone
ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W 1
8 P M. *Medicine* Dr T F Fox, Dr Hugh Clegg
Cooke, Dr W A R Thomson Comments
Editorial Chair
ST MARY'S HOSPITAL MEDICAL SCHOOL, Paddington, W
5 P.M Mr J D S Flew Induction of Labour
INSTITUTE OF DERMATOLOGY, St John's Hospital,
W C 2
5 30 P M Dr G C Wells Lupus Erythematosus

### Wednesday, 26th

ROYAL SOCIETY OF MEDICINE
5 P M *Endocrinology* Prof H L Sheehan, Mr D W C
field, Dr J E Caughey, Dr Oliver Garrod
Syndromes
INSTITUTE OF *LARYNGOLOGY AND OTOLOGY, 330, Gray's*
W C 1
5 30 P M Prof F C Ormerod Types of Deafness
INSTITUTE OF DERMATOLOGY
5 30 P M Dr J O Oliver Lupus Erythematosus
HARVEIAN SOCIETY 11 Chandos Street W 1
8 15 P M Dr R. Cove Smith Fitness—Facts and
(Presidential address)
BIRMINGHAM MEDICAL INSTITUTE, 154, Great Charles
Birmingham, 3
8 P M *Psychiatry* Dr Maxwell Jones Concept of
peutic Community

### Thursday, 27th

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn
W C 2
5 P M Mr H B Stallard Retinoblastomata treated by
Seeds and Radium Disks (Hunterian lecture)
BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P M (London School of Hygiene and Tropical
Prof C H Gray Chemistry of the Porphyrias
RENAL ASSOCIATION
4 30 P M (Ciba Foundation 41 Portland Place, W
D Innes Williams Dr R Pugh Renal
Dr S W Stanbury Dr M D Milne Base losing
LONDON JEWISH HOSPITAL MEDICAL SOCIETY
8 30 P M. (11, Chandos Street, W 1) Dr Macdonald
The Body Image
LIVERPOOL MEDICAL INSTITUTION, 114, Mount Pleasant,
pool 4
8 P M Dr A S Woodcock, Dr D G Miller Dr J H
Diagnostic Cytology
UNIVERSITY OF ST ANDREWS Medical School, Small's
Dundee
5 P M Dr J W Smith Postural Mechanism of Joints

### Friday, 28th

POSTGRADUATE MEDICAL SCHOOL OF LONDON Ducane Road
2 P M Mr B McN Truscott Carcinoma of the Female
4 P M Dr H S Banks Question and Answer on
Infectious Diseases
ROYAL SOCIETY OF MEDICINE
5 P.M *Pædiatrics* Dr Reginald Lightwood Dr Martin
Dr John Sutcliffe Eosinophilic Granuloma
Siwie Disease, Hand Schüller Christian Disease
INSTITUTE OF LARYNGOLOGY AND OTOLOGY
3 30 P M. Mr Maxwell Ellis Ulcers of the Mouth and
INSTITUTE OF DERMATOLOGY
5 30 P M Dr S C Gold Lupus Erythematosus
ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF
242, St Vincent Street Glasgow
5 P M. Dr E M McGirr Radioactive Isotopes

# Births, Marriages, and Deaths

## DEATHS

CASTELL.—On Jan 1 at Finchley, Samuel Percy Castell
M R.C.S aged 61

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Sir Allen Daley has been elected chairman of the
Association for Maternal and Child Welfare

The *British Journal of Anæsthesia* which last year was
every two months instead of as previously every quarter
to appear monthly

CORRIGENDUM *Tuberculosis in Immigrants*—In Dr
O Regan's letter last week (p 152) the first paragraph
" 85% of school leavers have been tested and vaccinated."
fourth paragraph the figures for Tipperary (N R.) should
"13 years 40%" (2145)

# THE DIAGNOSIS OF RHEUMATIC VALVULAR DISEASE

## 1924-1954 *

CRIGHTON BRAMWELL
M A. Camb M D Manc F R C P
SSOR EMERITUS OF THE UNIVERSITY OF MANCHESTER
CONSULTING PHYSICIAN TO THE MANCHESTER ROYAL INFIRMARY

-ONE before or since, has contributed so much as Coombs to our knowledge of the most important em in cardiology—the diagnosis and treatment of natic heart-disease His book on the subject hed in 1924 gave an admirably clear and authorita ccount of our views at that time Since then rer advances in radiology and in cardiac surgery o mention laboratory methods of investigation such onocardiography and cardiac catheterisation have n much new light on the picture and have consider modified our conception of valvular disease

rty years ago most cardiologists believed that the nical effect of valvular lesions was unimportant at what really mattered was the condition of the rdium. This was no new doctrine it had been the ng of George Balfour (1882) in Edinburgh and of m Steell (1906) in Manchester not to mention Mackenzie whose work, during the twenty five he practised in Burnley had convinced him that osis must be based on the patient s symptoms and the murmurs heard with the stethoscope With pinion I am sure we would all agree today but neither Mackenzie nor his contemporaries appre was that certain symptoms might be due to the mechanical effect of the valvular lesion

arding mitral stenosis Thomas Lewis wrote, in Although many symptoms may be complained patients suffering from actual stenosis, there are hat can be ascribed properly and usefully to this ity of the valve Since those words were written they are the words of one who was not only a l and accurate observer but also a lucid exponent views—we have learnt that in these cases, the nary congestion responsible for orthopnœa for rsmal dyspnœa, and for acute pulmonary œdema is y due to back pressure from mitral obstruc which can often be relieved by valvotomy with liate and remarkable benefit to the patient

noptysis has long been recognised as a common om in mitral stenosis but only in more recent as the importance of acute pulmonary œdema in ndition been fully appreciated We used to regard pulmonary œdema as a rare complication of mitral s, but now we know that this is not so It is in the most urgent indication for valvotomy My on was focused on this symptom in 1941 by two f mitral stenosis complicating pregnancy both of proved fatal The post mortem findings in these tients (Bramwell and Jones 1944) were illumin During life both had normal rhythm with a very rescendo presystolic murmur and at necropsy ere found to have severe mitral stenosis with great rophy of the wall of the left auricle This combina ggested that the rheumatic process had hit the ard, but spared the muscle Despite the extreme of stenosis the hypertrophied auricle had for years been able to maintain ventricular filling suddenly under the strain of pregnancy it failed ngs were flushed with blood pulmonary œdema ped and this rapidly proved fatal

It is in cases such as these with normal rhythm and a loud presystolic murmur that pulmonary œdema is most likely I believe the sequence of events, in such cases, is that a severe degree of mitral obstruction leads to a greatly increased left auricular pressure which in its turn calls forth a compensatory work hypertrophy in the auricular wall The powerful auricle ejects its contents with great force into the ventricle and the increased pressure gradient at the mitral orifice manifests itself clinically by the characteristic loud crescendo presystolic murmur Such hypertrophy occurs only when the auricular muscle is healthy a damaged auricle when subjected to strain fibrillates.

### Mitral Stenosis

#### THE MURMUR

Let me now refer to some of the physical signs associ ated with mitral obstruction the most important of which is the characteristic murmur

In the production of obstructive murmurs, two factors are concerned—the size of the orifice and the rate at which the blood is flowing through it. The one is static the other dynamic Further there is an inverse relation between the degree of stenosis and the velocity of the blood flow required to produce such a murmur

The influence of the dynamic factor is shown in fig 1 which is an optical record of the heart sounds and murmurs in a patient with mitral stenosis and partial heart block When we first listened to this patient s heart we were puzzled by the way the sounds and murmurs varied from cycle to cycle In the first cycle there is a loud first sound, but no murmur in the second the first sound is less loud but is preceded by a mid diastolic murmur with accentuation in auricular systole and in the third cycle where the ventricle failed to contract there is a loud murmur but no first sound The fourth cycle is similar to the first The absence of the presystolic murmur in the first and the last cycles is explained by the fact that both followed a missed beat and during the prolonged diastole preceding these cycles the auricle contracted twice When it contracted the second time it was unable to force sufficient blood through the mitral orifice to produce a murmur for the ventricle was already full During the intermission on the other hand the auricle contracted early in diastole and discharged its contents with considerable velocity into the empty ventricle producing a loud murmur The variability of the murmur in this case, was due entirely to the variation in the pressure gradient at the mitral orifice in different

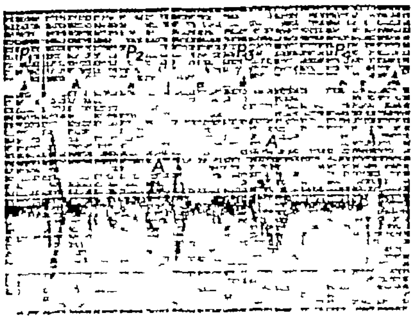

Fig 1—Electrocardiogram and optical phonocardiogram from a patient with mitral stenosis and partial A V block (This figure and the two following it, are reproduced from the *Quarterly Journal of Medicine* (1935 4 139) by courtesy of the Editors.)

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* Coombs lecture delivered at the University of Bristol Nov 23 1954

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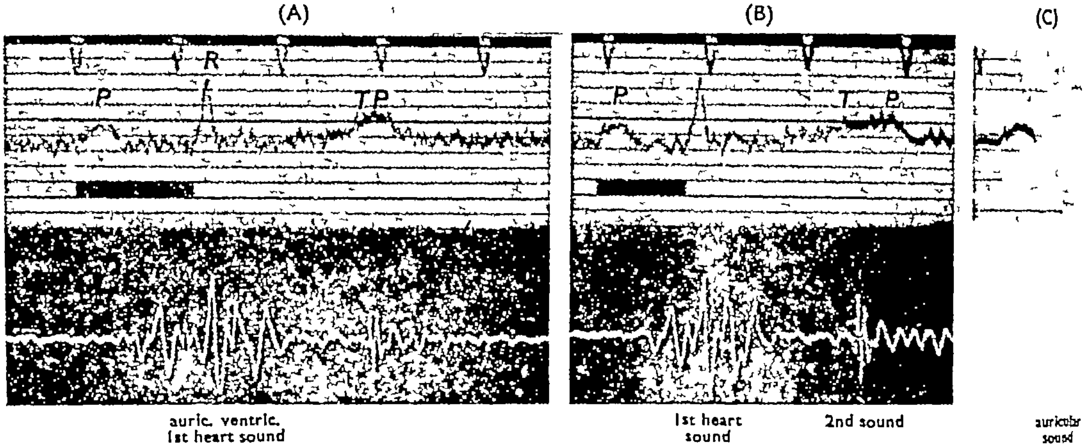

Fig 2—Electrocardiogram and phonocardiogram from a patient with partial A-V block (A) Cycle with prolonged P–R interval (B) Cycle with normal P–R interval (C) Cycle with isolated auricular contraction

cycles, as determined by intraventricular pressure at the time the auricle contracted

If the production of an obstructive murmur depends on the size of the orifice relative to the rate at which the blood is flowing through it, theoretically a murmur might be produced either by a narrowed orifice or by an increased blood flow, and we do in fact find that, in subjects with a normal mitral orifice, when the cardiac output is increased by exercise, or when the heart is overactive, as in hyperthyroidism, the first heart sound bears a close resemblance to that of mitral stenosis (Bramwell 1943) There is, then, what we might call a physiological, as opposed to an anatomical, stenosis This was clearly recognised by Carey Coombs, who stated that " A colourable imitation of a presystolic murmur is sometimes perpetrated by a normal heart acting fast "

Paul Wood (1950) has pointed out that the apical diastolic murmur heard in some patients with a patent ductus disappears when the ductus is tied This murmur is indistinguishable from that of mitral stenosis and is obviously due to an increased blood-flow through a normal mitral orifice

The reason for the crescendo character of the presystolic murmur has been a matter of some controversy Personally I believe that it is due to the final vibrations of the murmur being superimposed on, and reinforced by, the initial vibrations of the first heart sound In patients with partial heart-block, in cycles where the P–R interval is prolonged, the complete auricular complex (which is identical with the sound picture in isolated auricular beats) precedes the vibrations of the first heart sound, but, when the P–R interval is of normal length, only the initial vibrations of the auricular sound complex can be seen, the later vibrations being obscured by those of the first heart sound (fig 2)

Likewise, in patients with mitral stenosis and auricular fibrillation, when two cycles follow one another in quick succession, the murmur completely fills diastole it runs right up to the first heart sound, and, to the ear, has a crescendo character, like the auriculo systolic murmur But when diastole is longer there is a silent interval between the murmur and the succeeding first heart sound (fig 3) Under these circumstances the murmur has no crescendo termination

### THE PULMONARY SECOND SOUND

In addition to the murmurs we have been considering, there are certain other important auscultatory signs of mitral stenosis Let me refer first to accentuation and [illegible] of the pulmonary second sound

Accentuation of the pulmonary second generally attributed to increased pressure in th ary circuit, but that this is not always the true tion is shown by the fact that a loud second the pulmonary area is sometimes heard in patie pulmonary stenosis, in whom the pressure in the ary artery is lower, not higher, than normal The tion, in such cases, is that the second sound up of two components, the one due to closure aortic and the other to closure of the pulmonar The loud second sound in the pulmonary area, in with pulmonary stenosis, is due not to the pul but to the aortic component It is in fact not ac tuated pulmonary second sound that we hear accentuated aortic second sound in the pulmon Abrahams and Wood (1951) have shown that in pulmonary stenosis the pulmonary component second sound is absent

In most healthy children and young adults components can be clearly distinguished—that is the second sound is split Normally the aortic closes before the pulmonary, and in cases of incompetence, owing to the shortening of left ven systole, the two components of the second sound more widely separated (Brigden and Leatham Conversely, in patients with left bundle branch left ventricular systole is delayed and the p precedes the aortic component of the secon (Wolferth and Margolies 1935)

The split second sound is always best heard pulmonary area, and in some cases cannot be elsewhere

### THE OPENING SNAP

" Reduplication " of the second sound at has been recognised since the time of Bouillau as an important sign of mitral stenosis That tional sound was produced at the mitral orifice, not due to asynchronous closure of the aortic monary valves, was appreciated by Potain

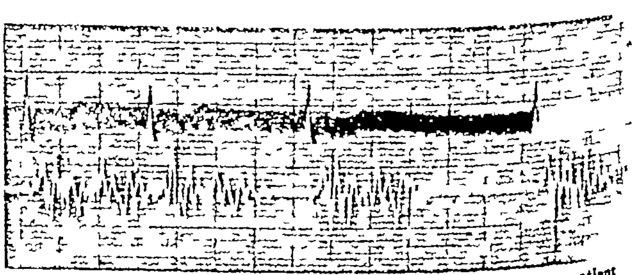

Fig 3—Electrocardiogram and optical phonocardiogram from a patient stenosis and auricular fibrillation

ave coined the term 'claquement d'ouverture de la ale' Margolies and Wolferth (1932) were able by hic records, to differentiate this 'opening snap' n the split second and from the third heart sound, and how that it was synchronous with the opening of the al valve

linically it is generally possible to distinguish the ning snap from the physiological third heart sound which I shall refer later) by its character site of imal intensity, and timing The opening snap is p and high pitched resembling in quality the second t sound, whereas the third heart sound is longer lower pitched The opening snap is usually loudest point between the apex and the left sternal border lightly higher up while the third sound is best heard the immediate vicinity of the apex The opening usually occurs earlier in diastole than the physio cal third heart sound the average interval after the mencement of the second heart sound being according to Mounsey (1953) 0 07 sec and 0 20 sec respec ly Unfortunately as Wood (1954) has pointed out, dvanced mitral incompetence the third sound may ome much more like an opening snap in that it may ess delayed and much sharper and higher pitched n usual

ellors and his colleagues (1953) believe that the ening snap is due to sudden tension of the mitral e as it balloons upwards into the ventricle at the t of diastole and consider that it is a reliable sign of re mitral stenosis with a pliant diaphragmatic type valve It is absent when mitral regurgitation is dominant and when the valve is much calcified (Wynn ) and for these reasons it may be regarded as a urable indication for valvotomy

ikewise Sellors and his colleagues think that the racteristic snapping first sound (which they call the sing snap') is due to sudden tension of the pliant al diaphragm as it bulges into the auricle at the nning of systole This closing snap can be palpated ell as heard In the words of Carey Coombs The l placed over the precordium feels the apex bang lenly and sharply against the chest wall then sink y from it as suddenly as it arrived

## THE THIRD HEART SOUND

gallop rhythm, three instead of two heart sounds mpany each cardiac cycle the additional sound t due to rapid distension of the ventricle When the ional sound is synchronous with auricular systole convenient to call it the fourth heart sound (Evans ) to distinguish it from the third heart sound which s early in diastole

here are three types of gallop rhythm of clinical rtance—protodiastolic, presystolic and summation p (fig 4) In protodiastolic gallop the additional d is an accentuated third heart sound, in presystolic p it is the fourth heart sound and in summation p it is a combination of the two for when the heart ting quickly auricular systole falls in early diastole the result that the third and fourth heart sounds ide

systolic and summation gallop do not concern us but protodiastolic gallop merits careful considera for it occurs in normal subjects as well as in patients mitral disease

yer (1908) found that a third heart sound was le in 68% of healthy young persons He also nstrated experimentally in dogs a similar sound corresponded in time to the sudden distension of entricle th[illegible]rred early in diastole and he ested that [illegible] heart sound was due to the n rush o[illegible]om auricle to ventricle when itral valv[illegible]ns

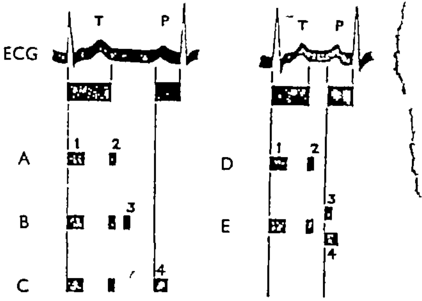

Fig 4—Diagram to illustrate different types of gallop rhythm. (A and D) Normal rhythm. (B) Protodiastolic gallop (C) Presystolic gallop (E) Summation gallop. 1 2 3 4 First second third and fourth heart sounds. The large rectangles immediately below the electro cardiogram represent ventricular and auricular systole.

So many apparently healthy recruits were referred to me during the war by the Ministry of Labour and National Service on account of a third heart sound that I decided to investigate the matter In a consecutive series of 832 recruits examined a third heart sound at the apex was heard in 151 This series did not include any case in which a diastolic murmur could be heard or a presystolic could be elicited exercise

The incidence of the physiological third heart sound is greatest in young subjects. It was present in 43% of men under 20 but in only 10% of those over that age

In mitral regurgitation the rate of ventricular filling is increased This favours the production of a third heart sound Severe stenosis has the opposite effect Hence in patients with mitral disease there is likely to be an opening snap but no third heart sound when stenosis predominates but a third heart sound and no opening snap when incompetence is the dominant lesion

I cannot leave this subject of mitral stenosis without referring to the murmur of pulmonary incompetence associated with the name of my old teacher Graham Steell Steell's (1888) original description of this murmur which he called "the murmur of high pressure in the pulmonary artery' was a masterpiece of clinical observation He drew attention especially to the variability of the murmur from day to day and to its constant association with a greatly accentuated pulmonary second sound

The Graham Steell murmur is now accepted by all cardiologists but the same cannot be said of the Austin Flint (or what a candidate I examined in Membership called the Austin Reed murmur! It wasn't till I asked him who Austin Reed was that I thought I could perceive a faint flicker of activity in a remote corner of his temporal lobe )

The original description of this murmur (Flint 1862) was based on two cases of aortic incompetence in which an apical presystolic murmur had been audible during life but no disease of the mitral valve was found at necropsy Flint suggested that the regurgitant stream through the aortic orifice impinged on the aortic cusp of the mitral valve and brought the leaflets of the valve into apposition causing a functional stenosis of the mitral orifice Paul White (1926) put forward the alternative hypothesis that the murmur was due to relative stenosis of the mitral orifice following dilation of the left ventricle Some workers however including Warburg (1946) and Luisada (1944) are doubtful whether such a murmur ever occurs and Carey Coombs himself appears to have been of that opinion He wrote In very few [illegible] indeed does there seem to be incontrovertible of the Flint hypothesis.

### Mitral Incompetence

No valvular lesion has had quite such a chequered career as mitral incompetence Those who served in the first world war were well acquainted with "V D H" (valvular disease of the heart) and "D A H" (disordered action of the heart) These two terms made cardiology delightfully simple If you heard a murmur it was V D H , if you didn't, it was D A H Now V.D H was organic, but D A H was functional , so, if a man had V D H he had to be invalided out, but if it was only D A H he could be cured and returned to duty ! The diagnosis of V D H was perhaps not quite so fantastic as might appear at first sight , for we were dealing with young men, and the only common types of heart disease in this age group are rheumatic and congenital, both of which generally manifest themselves by murmurs Coronary disease and hypertension do occur, but they are exceedingly rare at this age Where this diagnosis came to grief was the failure to recognise that heart murmurs might be due to causes other than valvular disease

Graham Steell (1906) gave credit to his "master," George Balfour of Edinburgh, for being the first to point out that, in chronic "mitral disease" the condition found post mortem was commonly mitral stenosis, not structural damage to the valves producing incompetence without stenosis Steell states that, at that time, the terms "mitral disease" and "mitral incompetence" were practically synonymous Balfour (1882) had realised that mitral regurgitation was not necessarily due to a damaged valve, and had coined the term "curable mitral incompetence" for the systolic murmur heard in cases of chlorosis—a murmur which disappeared when the anæmia was successfully treated

Steell himself emphasised the fact that muscle contraction was an essential complement of the valvular apparatus In his own words, "No mitral valve can be competent if it fails to receive that assistance from the heart muscle it is designed to receive in the performance of its function" He added "Such destruction of the mitral curtains as would alone cripple their function (without there being mitral stenosis) is almost limited to cases of septic endocarditis" To this last statement I shall refer again later

Regarding this point, Carey Coombs wrote "An apical systolic murmur is certainly an indication of mitral incompetence , but, unless the bruit be long, loud and high pitched, it does not prove that the incompetence is due to endocarditis and it should be attributed to muscular rather than valvular disease"

Nevertheless in 1914 this lesson had not been driven home, and, in the first world war, many doctors had still to learn that a heart murmur did not necessarily mean valvular disease

Between the two wars, the pendulum swung in the opposite direction—obviously too far Some cardiologists of this period seemed to regard the diagnosis of "mitral incompetence" as hardly decent ! Lewis (1933) wrote "There are no symptoms to be attributed to mitral regurgitation The only sign that can be named is a systolic murmur" Cabot (1926) in his fascinating book *Facts on the Heart*, in which he correlates the clinical with the post mortem findings, recognises that mitral incompetence may occur, but concludes that a diagnosis of mitral regurgitation without stenosis is never justified

Freeman and Levine (1933), on the other hand, believed that loud apical systolic murmurs were generally due to mitral disease, and both Fishberg (1940) and Master (1948) held that the importance of apical systolic murmurs had been underestimated

The successful intervention of the surgeon in the treatment of mitral stenosis gave a new lease of life to mitral incompetence , for, although rheumatic mitral [illegible] ce without stenosis is rare, a combination [illegible] s common, and in assessing the suitability of a case for valvotomy it is important to know wh predominant

We now base the diagnosis of mitral regurgit chiefly on three signs (1) a loud apical systo (2) dilatation and hypertrophy of the left ven which is recognised clinically by the heaving su apical impulse, and radiologically by the charac changes in the cardiac silhouette described by P (1949) , and (3) expansile pulsation of the left synchronous with ventricular systole This can b in the postero-anterior as well as in the right o position, and must be distinguished from bac displacement of the left auricle by a hypertroph ventricle, which may occur in pure mitral stenosis sign is not always present Confirmatory evidence be obtained from the pulse, which in mitral incomp is of full volume as contrasted with the small pulse of pure stenosis

Nevertheless, as Baker and his colleagues (1959 pointed out, despite these various diagnostic cr unsuspected free mitral regurgitation is occa revealed at operation

Douglas and Hill (1954) compared the clinical ment of mitral incompetence with the operative In 26 cases in their series there was close agreement 5 cases mitral incompetence was suspected but stenosis was found at operation , while in 15 case degree of mitral incompetence was underestimated

BACTERIAL ENDOCARDITIS

I have already referred to the association of pure incompetence with bacterial endocarditis This as tion is well recognised, but has never been satisfac explained Of Brigden and Leatham's (1953) se 30 cases of pure mitral incompetence, 10 had ba endocarditis , and of my own (Bramwell 1948) se 12 cases of bacterial endocarditis with mitral that came to necropsy, mitral stenosis was pres only 2 So rarely does one hear a typical cre presystolic murmur in patients suffering from b endocarditis, that its presence is sufficient to m question the correctness of the diagnosis

These facts cannot fail to raise in one's mind whether the orthodox view that subacute ba endocarditis rarely attacks a heart not prev damaged by rheumatic infection, or the seat of congenital abnormality, is correct , for it is rem that the pre existing heart disease is almost trivial, and that patients with advanced heart appear to be relatively immune For example, au fibrillation was present in only 5 of Cates and Ch (1951) 269 cases Likewise of the 33 patients in r series, none gave a history of heart-failure before tion, and in only 3 had there been any con impairment of capacity for effort

Some observations by Carey Coombs have an tant bearing on this subject In 1923 Coombs re 30 cases of "endocarditis lenta" seen since the e first world war He distinguished "endocarditis from the more acute type of bacterial endocar the facts that it runs a course of many months years (one of his patients lived for over three that there is little or no fever, and that necrops anatomical evidence of stubborn opposition infection

Of his 30 patients, 29 were males, of whom served in the Army, and of these 80% had been men or gunners, with an average period of se more than three years, mostly in France Coor that, with only one exception, they were "me physique and morale, men who joined the arm served with all their might, and [illegible] them the utmost limit of their physical [illegible]" Br he did not encounter a single case among men of ysique whose service had been at the base and ere at home or overseas He concludes that So nt is the relation/between physical fitness and ous exertion on the one hand, and proneness to rdial infection on the other that a belief in the relation between the two can hardly be avoided ggests that excessive fatigue from the strenuous on to which these men had been subjected may redisposed the body to infection It is indeed hard eve that these men had any pre existing valvular

## Aortic Stenosis

views regarding the diagnosis of aortic stenosis been profoundly modified in recent years

### SYMPTOMS

1933 Thomas Lewis wrote ' There are no symp of aortic stenosis. ' It is interesting to compare this nent with that of King nine years later (Bramwell ing 1942) He wrote

> tients with this condition are liable to the usual symp- f cardiac disease and in addition they frequently show e of cerebral anæmia Angina may occur Sudden n is poorly borne and may be followed by sharp dyspnœa ncope When the heart begins to fail the progress is persistently downhill regardless of therapy The r very often proves fatal during the sixth decade later stages, mild mental symptoms are common : lity extreme drowsiness and delusions

surprising how many of these patients remain free symptoms until the sixth or seventh decade in of having led active lives Not infrequently a ur had been noted many years previously This l picture which has been well described by David (1951) does not seem to have been familiar to ians in the past. Lewes s paper is based on 25 of calcareous ' lone aortic stenosis verified post n (i.e., cases in which aortic stenosis was the only ant valvular lesion)

age at which symptoms develop in these cases ts that they are not directly due to the pre-existing ar lesion which may be of long standing but to degenerative changes superimposed upon it have transformed it from a benign to a malignant ion just as subacute bacterial endocarditis may rimposed upon rheumatic mitral or aortic valvular

mechanism of syncope in these patients has not nally established : it differs from ordinary vagal o in that it is usually associated with effort and respect it resembles angina of effort Moreover ersten (1951) found that, in patients with severe stenosis who developed syncope cardiac pain was more common than in those who did not Likewise and Bean (1948) found that sudden death in s with aortic stenosis was most common in those lso experienced cardiac pain This apparent tion between syncope and sudden death on the nd and cardiac pain on the other suggests that ay be due to the same cause—namely myocardial ia—a hypothesis which receives support from ersten s further observation that of patients with stenosis those who develop syncope have larger and so would be more liable to ischæmia than who do not Contratto and Levine (1937) have l out that in these cases cardiac pain may occur ndently of aortic incompetence or coronary

s been shown by Tennant and Wiggers (193[illegible] hat myocardial ischæmia leads to a dim[illegible] output and Hammersten suggests acc[illegible] ncope may be due to cerebral anæmia [illegible] iminished cardiac output secondary to m[illegible] ia

### PHYSICAL SIGNS

Regarding diagnosis Thomas Lewis wrote

> The outstanding diagnostic sign of aortic stenosis is a small pulse rising slowly to a delayed summit : the condition should never be diagnosed without this sign The second sign is a systolic thrill at the base of the heart usually maximal at the second right cartilage or space

Our diagnostic criteria are now much less rigid than they were then for Wiggers (1944) has shown that it is not until the aortic orifice is reduced to a quarter of its normal size that the form of the pulse is modified in the manner described by Lewis It is therefore hardly surprising that this sign is present in less than half the cases. Even in severe stenosis, the pulse may be full and collapsing and in about half the cases there is some associated aortic incompetence

A loud harsh basal systolic murmur is the commonest sign in these cases , in fact it may be the only sign The murmur, however is not always loud , and, unless it is loud, there is no thrill Moreover the murmur is often well heard not only at the base but also at the apex and occasionally is loudest in that area in which case it may not be easy to decide whether it is due to aortic stenosis or to mitral incompetence for both lesions give rise to left ventricular enlargement, and in both the pulse may be of full volume Under these circumstances, as Leatham (1951) and others have shown the shape of the systolic murmur and its relation to the heart sounds in the phonocardiogram may be helpful in diagnosis In aortic stenosis the systolic murmur [illegible] shortly after the first sound and rises to a max[illegible] mid-systole It then diminishes rapidly [illegible] before the second sound In mitral incomp[illegible] other hand the murmur fills the whole of [illegible] immediately after the first sound and [illegible] up to the second sound which may be [illegible] the apex if the murmur is loud

Absence of the aortic second sound [illegible] able importance in diagnosis has [illegible] been attached is evidence of advanced [illegible] but as Parkinson and Hartley (1946) [illegible] a normal second sound does not exclude the [illegible]

Parkinson (1949), in his Ca[illegible] empha sised the value of fluoro[illegible] of this lesion It reveals n[illegible] of the left ventricle but also calc[illegible] of the aortic valve Tomography can also be [illegible] calcification (Davies and Steiner 194[illegible] was present in 26 of the 32 cases [illegible] to and Levine (1937)

Campbell and K[illegible] find any consist[illegible] relation in their cases [illegible] of the [illegible] second sound [illegible] of the valve [illegible] in

Another [illegible] fluoroscopy the [illegible] tance of which has been emphasised by Kiloh (19[illegible] with others [illegible] ascending aorta [illegible] others in the [illegible] 1949) also [illegible]onchiectasis

### [illegible]TIOLOGY

[illegible] of calcific a[illegible] d proved and [illegible] divided Kar[illegible] and 4 2% of (19[illegible] monograph [illegible] 11 children [illegible] came to the [illegible] unsatisfactory [illegible] always rheu[illegible] ho eventually [illegible] strongly [illegible] minate [illegible] 1921 1936) [illegible] non-specific [illegible] He Kiloh [illegible] aortic stenosis [illegible] of age wa[illegible] rheumatic [illegible] aortic sten[illegible] incompetence or [illegible] this view pathological as well as clinical, points to the extreme rarity of aortic stenosis as a result of rheumatic infection "

Rheumatic carditis generally leads to stenosis of the mitral valve, but to incompetence of the aortic valve, and I would suggest that the reason for this is purely anatomical the cusps of the mitral valve spring from a continuous curtain, so, when cicatricial contraction follows inflammation, they tend to be drawn together, whereas the cusps of the aortic valve are discrete, and so tend to be drawn apart

When calcification supervenes in a case of pure aortic stenosis, the valve may become incompetent, but, in rheumatic disease of the aortic valve, stenosis is secondary to incompetence

The sex-incidence of calcific aortic stenosis (males being affected much more commonly than females), its benign course over a long period of years, the rarity of a history of rheumatic infection, and the fact that it is hardly ever associated with a mitral lesion, are all strongly opposed to the idea that the condition is rheumatic

In a recent paper, Campbell and Kauntze (1953) point out the difficulty in arriving at a histological diagnosis in cases with scarred and calcareous aortic valves, and consider that the ætiology may be more accurately assessed from the history, progress, and physical signs than from necropsy material They believe that pure aortic stenosis under the age of 30, is more likely to be congenital than rheumatic In 20 of their 40 cases, the heart murmur was noticed in early childhood, generally before the age of 4, and many of their cases were referred to them with a diagnosis of congenital heart disease

Campbell and Kauntze make the interesting observation that many of these patients, like patients with coarctation of the aorta, have outstandingly good physique

Compared with the other three valvular lesions we have been considering, aortic incompetence has attracted very little attention during the past thirty years in fact I think it would be true to say that Corrigan's (1832) original description of the clinical picture has scarcely been modified by subsequent work

## Conclusion

My aim here has been to review certain aspects of the changing picture of rheumatic valvular disease

The remarkable advances which we have witnessed in cardiac surgery in recent years have aroused a new and lively interest in mitral stenosis, and improvements in phonocardiographic technique have enabled us to record with greater accuracy what we hear with the stethoscope Just as electrocardiography, by depicting the various types of arrhythmia, enabled us to recognise them by the unaided senses, so phonocardiography is teaching us to distinguish, by auscultation, between the different sounds and murmurs heard in health and disease

In the period between the two world wars, mitral incompetence was regarded by most cardiologists with remarkably little respect since the introduction of mitral valvotomy, however, its importance has been universally recognised, though its clinical recognition is not yet always possible

The radiological diagnosis of valvular calcification has widened our concept of aortic stenosis, but the ætiology of this condition, and the mechanism of production of some of the symptoms associated with it, are still undetermined

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# PULMONARY PRIMARY TUBERC IN CHILDHOOD

C H M Walker
M.D Edin, M.R C P., D C.H.
SENIOR REGISTRAR TO THORACIC UNIT, THE HOSPITAL F
CHILDREN, GREAT ORMOND STREET, LONDO

THE belief that the prospects of all childr healed primary tuberculosis are universally go been questioned by Holmdahl (1950) in Scandin only a long-term follow-up will tell whether or th same prognosis holds good for this country Th is the preliminary report of such a follow up R publications by Bentley et al (1954) and Holmdahl are accompanied by comprehensive bibliographies need not be repeated here extensively

## Material

The number of children examined in the pres was 767, comprising 719 examined in the outpatient clinic and in the wards of the Hospital f Children, Great Ormond Street, and 48 seen at U College Hospital, London This number does no sent all the Mantoux-positive children atten hospitals but only those whose clinical picture tuberculosis and who were radiographed because Of these, 102 were considered to be no longer " judged by general condition, erythrocyte-se rate (E S R ), and radiological appearances In 53 the site of the primary complex could not be dete and 34 showed evidence of non-pulmonary These were all excluded from this analysis, lea cases in which there was adequate evidence of a primary tuberculous complex in the lung wh examined This unfortunately cannot be regar truly random sample of patients with this co

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se there was, in the early days of streptomycin y a high admission rate of children with tubercu eningitis sometimes in the later stages Some such en were admitted from other hospitals and others eferred by general practitioners and tuberculosis or were diagnosed in the course of general medical ient work It is realised also that hospitals of this of necessity see more ' complicated ' cases than a act' or tuberculosis chest clinic

number of cases included in each analysis varies ding to the information available the duration of up and the type of treatment Any particular on is explained in the appropriate section

### Complications of Primary Complex

he 578 cases 40 were omitted from this analysis e of inadequate documentation Half of the ing 538 children were followed up for two years re, and rather less than a half of these are still observation About 20% (106) were followed e or two years and 12% for from six months ear This leaves only 18% of the children who ollowed up less than six months They include se, most of the 55 who died and since relatively hers were followed up so short a time the analysis below of the complications which may follow the ary primary complex must be fairly accurate I)

*ntal Lesions*

workers agree that the most common compli of the primary complex is the segmental lesion adiologically yet the incidence of this finding widely in different reports Macpherson and che (1950) report a collapse incidence of 4.7% y et al. (1954) and Roberts and Blair (1950) 19% hompson (1952) 28% Such differences are not rising when one considers for example that Miss erson's cases come from a contact clinic and Dr y's from a residential institution. One might the more severely complicated cases to be admitted pital treatment and thus an unavoidable selection s is made.

s been found also that the age of onset has some on the frequency of collapse Richards (1944) that 21% of 239 children aged less than 6 years llapse due to bronchial obstruction and only f children aged more than 6 years

other possible explanation for this discrepancy found in the interpretation of the radiological tal shadow Adler and Richards (1953) think llapse and consolidation can be distinguished gically, but most workers find this distinction if not impossible What exactly is meant by rms as epituberculosis and flare is uncer d the criteria for the selection of a specific lesion collapse are difficult to establish Epituberculosis a diagnosis we no longer recognise and because confusion of nomenclature and difficulty of inter n the remaining group of collapse consolidation called hilar flare have been classified under one in the present series It is fully realised that in re must have been caseating pulmonary lesions and this has been borne out by the later appear calcification in the lung parenchyma or by ny specimens On the other hand, the gradual of an obstructed bronchus confirmed by repeated scopy and a coincidental clearing of the radio- shadow were seen often enough to convince us lapse is the main feature in most cases

therefore because of this classification and the ty of the cases that the incidence of this seg lesion is as high as 48.3% (260/538) in this series re differs strikingly from the over all incidence of suggested by Bentley et al. (1954)

TABLE I—COMPLICATIONS IN 538 CHILDREN

| Complication | Age at onset (yr) | | | Total |
|---|---|---|---|---|
| | 0–2¹¹/₁₂ | 3–5¹¹/₁₂ | 6–12 | |
| Collapse consolidation &c. | 96 | 98 | 66 | 260 (48.3%) |
| Local dissemination | 12 | 7 | 6 | 25 (4.6%) |
| Proved bronchiectasis | 1 | 5 | 5 | 11 (2.0%) |
| Pleural effusion | 3 | 9 | 16 | 28 (5.2%) |
| Meningitis | 19 | 16 | 6 | 41 (7.6%) |
| Meningitis and miliary tuberculosis | 10 | 14 | 6 | 30 ([illegible]) |
| Miliary tuberculosis only | 13 | 5 | 4 | 22 (4.1%) |
| None | 48 | 53 | 64 | 165 (30.7%) |

*Local Parenchymatous Dissemination*

This may well have been present in some cases, but definite radiological evidence was only obtained in 10 of the survivors the total incidence being 4.6% (25/538) We came to regard this complication along with cavitation and bronchopneumonia with some trepidation because the mortality rate in the lowest age group (0–2 yr 11 mos ) was about 60% Among the survivors there were 5 in whom cavitation was observed but it has been suggested that more frequent tomography would reveal a greater incidence of this complication (Heaf 1953) The necropsy figures of Bentley et al. (1954) add weight to this suggestion

Most workers—e.g Hardy et al 1952 Daly et al. 1952 Lowys and Larmoyer 1953 Carlens and Hellström 1953 Adler and Richards 1953—find endobronchial disease in about half the cases bronchoscoped with fistulæ less often observed and the results in the present series are no exception The bronchial wall was breached and the lumen encroached on by caseous material in 20 of 44 children bronchoscoped It is therefore perhaps surprising that bronchopneumonia is rare occurring only three times amongst the survivors and eight times in 58 necropsies Gemini and Rickler (1952) consider that most fistulæ heal without spread of tuberculosis

*Obstructive Emphysema*

This developed in only 7 children and is particularly mentioned because at first this complication of hilar adenitis may be missed It is usually associated with particularly large glands which have ulcerated through into the lumen of the bronchus Stridor is often a prominent symptom, and bronchoscopy may give considerable relief

*Bronchiectasis*

The development of this complication has always figured largely in published reports and in this country Roberts and Blair (1950) Jones et al (1940) and Hardy et al. (1952) have reported an alarmingly high incidence 60% 70% and 71% respectively of children with segmental lesions were found to have bronchiectasis in most cases confirmed by bronchography Daly et al (1952) however found only 1.1% of 434 children with tuberculosis had proved bronchiectasis but 18 others were suspected of having it Hutchison (1949) also found a low incidence 2 cases developing bronchiectasis out of 30 showing collapse

In the present series 11 children had proved and persistent bronchiectasis—i.e. 2% of 538 and 4.2% of the children with segmental lesions Of these 11 children 5 were among the 7 whose progress was unsatisfactory whose lesions persisted for years and who eventually underwent lobectomy This may be an underestimate and more cases may manifest themselves later but there is good reason to believe that the early bronchial dilatation associated with segmental collapse is reversible If bronchography is done early in the disease while collapse is present a high incidence of bronchial dilatation may be expected but good filling of the bronchial tree may at this stage of the disease be difficult. Even though some dilatation remains after re-expansion it is usually symptomless (Jones et al 1940 Williams and Anderson

TABLE II—DEATHS (INCLUDING NON-PULMONARY PRIMARY CASES)

| Complications | Age (yr) | | | | | |
|---|---|---|---|---|---|---|
| | 0–2¹¹/₁₂ | | 3–5¹¹/₁₂ | | 6–12 | |
| | No of cases | No of deaths | No of cases | No of deaths | No of cases | No of deaths |
| Tuberculous meningitis | 19 | 11 (*58%*) | 19 | 6 (*32%*) | 6 | 1 (*17%*) |
| Tuberculous meningitis and miliary tuberculosis | 22 | 16 (*73%*) | 14 | 11 (*79%*) | 9 | 5 (*56%*) |
| Miliary tuberculosis | 14 | 6 (*43%*) | 8 | 0 | 5 | 1 (*20%*) |
| Total | 55 | 33 (*60%*) | 41 | 17 (*41%*) | 20 | 7 (*35%*) |

1953), and it is for this reason that bronchography was not done more often in children with segmental lesions Until a few years ago bronchograms were done simply to confirm the presence of bronchial dilatation Latterly, however, they have been done only if the children have remained ill and have shown persistent physical signs for two or more years These children are among the important few who eventually require operation, and up to date 5 of the 11 children with proved bronchiectasis have had lobectomies Altogether 39 children showed suspicious bronchial markings on straight radiography, and 16 of them underwent bronchography 10 showed dilatation, 5 showed a normal bronchial tree, and in 3 the procedure was unsuccessful Most of these children showing some crowding of the bronchi and suspicious dilatation were radiologically normal in about two years, but it seems that those who have abnormal bronchograms after this time are likely to require surgery In addition to the 5 who have already had lobectomies, at least another 2 will probably require surgical treatment

*Pleural Effusion*

As might be expected, half (57%) of the 28 children with this complication were in the oldest age group (6–12 years), but 3 cases occurred in children aged less than 3 years, and 12 in children aged less than 6 years

There have been reports that the ultimate prognosis of tuberculous pleural effusion is considerably worse than that of the simple primary complex (Bentley et al 1954, Smithers 1934), and that children who develop their effusion after the age of 10 years have higher morbidity and mortality rates than the younger patients (Nathorst 1948) The long-term follow-up of these 28 children may be of some further value in this respect

*Miliary and Meningitic Tuberculosis*

These were the most serious complications and either separately or together accounted for most of the deaths in this series (table II) There were 102 cases (19%) The incidence of these conditions alone or in combination is seen in table I Of 61 children with miliary tuberculosis more than half developed meningitis, and, as in the investigation of 100 deaths by Bentley et al (1954), there were about the same number of cases of meningitis with as without miliary disease Again, as one might expect, the incidence of meningitis is highest in the lower two age-groups—i e, less than 6 years—though miliary tuberculosis alone was much more often found in the children aged less than 3 years

It must be emphasised again that the incidence of these serious complications is high partly because the cases admitted to hospital are a selected group, but the proportions within this group can probably be regarded as true estimates for hospital practice as a whole

*Miscellaneous Complications*

To complete the picture the following complications mentioned, if only to indicate what diverse results may ensue through a restricted hæmat spread subcutaneous abscesses, dactylitis, spinal arthritis of the hip, lupus, skin tuberculides, ma and tuberculoma We have been impressed b late after the active phase of the primary comple tuberculosis can develop, and how easily the earl of such a severe condition as spinal caries can be

Phlyctenular conjunctivitis (unlike erythema n which is seen only in the early phase) has been at all stages of activity of the primary comp in 1 case the pressure of an enlarged gland phrenic-nerve palsy

### Bacteriology

The isolation of the tubercle bacillus is still and chancy The advances in homogenising such examination have unfortunately little bea pædiatric practice, and the Ministry of Health has pointed out how important is the lab nique With the advent of B C G the finding bacillus has become more important, and it appointing to find such a high percentage of results in children known to have primary tub This is not really surprising, since the primary is virtually a closed lesion, unless there parenchymatous spread or ulceration into a

The results of bacteriological investigations cases are shown in table III If the figures for th and adenoids are excluded, positive results we in only 16% of examinations (25/152) This at fi seems to compare unfavourably with the 30% of Bentley et al (1954), till it is realised th patients included adolescents and a greater

TABLE III—BACTERIOLOGY

| Source | Age (yr) | | | | |
|---|---|---|---|---|---|
| | 0–2¹¹/₁₂ | | 3–5¹¹/₁₂ | | |
| | Positive | Negative | Positive | Negative | Po |
| Pleural fluid | | 3 | 1 | 6 | |
| Sputum | | | | 6 | 1 |
| Stool | 1 | 12 | | 2 | |
| Gastric washing | 12 | 43 | 5 | 17 | 5 |
| Tonsils | 4 | 7 | 1 | 3 | 1 |
| Adenoids | 7 | 2 | 3 | 1 | 1 |
| Tonsils and adenoids together | | 10 | | 10 | |

patients with chronic pulmonary tuberculosis, fro sputum is more easily obtained The perc positive gastric washings in their cases and in th series, however, is the same—about 22% T comparison might be expected because gastr would be used in children of much the same age a similar clinical picture in the two group examination of pleural fluid and stools reward, the discovery of the tubercle bacillus closely related to the availability of sputum sputum is obtained, however, there is still chance of isolating the bacillus, even in older chi adolescents

The tonsils and adenoids were removed in 64 reasons which include chronic nasal discharge, infection of the upper respiratory tract which with the child's general progress, sometimes phlyctenular conjunctivitis, and because examination showed that infected tonsils and could keep the E S.R raised and delay the heal chest lesion

The tonsils often looked unhealthy, but tonsils just as often look innocent (Browne 1952) In no case was there tuberculous cervical yet in 17 (26%) of 64 examinations of tons adenoids evidence of tuberculosis was seen on examination Browne and Hall (1952) found the

LE IV—SOURCE OF INFECTION IN 578 CASES

| s | Age (yr ) | | | | | | Total |
|---|---|---|---|---|---|---|---|
| | $0–2^{11}/_{12}$ | | $3–5^{11}/_{12}$ | | 6–12 | | |
| | Definite | Doubtful | Definite | Doubtful | Definite | Doubtful | |
| | 40 | 5 | 20 | 1 | 30 | 5 | 110 |
| | 21 | 6 | 19 | 5 | 16 | 1 | 69 |
| nt | 1[illegible] | 1 | 12 | 2 | 7 | [illegible] | 36 |
| rela- | 21 | 2 | 30 | 2 | 20 | 3 | 81 |
| ple | 11 | 3 | 14 | 3 | 13 | 1 | 45 |
| | 130 | | 111 | | 100 | | 341 |
| not | 64 | | 103 | | 99 | | 260 |

ere obtained from the tonsils and adenoids in third of the active, and in none of the inactive primary tuberculosis of the lung In the absence l adenitis it is likely that the tonsils and adenoids ondarily infected by tubercle bacilli from the l secretions If there is chronic infection of the spiratory tract the removal of the tonsils and is probably justified because there is a 1 in 4 hat these may act as a source of continued with tubercle bacilli

## Source of Infection

the 578 children had a history of contact with case of tuberculosis 29 of them having had contacts (table IV) The remaining 260 children uch history and only very few of these had no f the question having been asked. Over half lren (54%) therefore had a tuberculous contact er (not the mother as might be expected) being common positive contact It is not surprising the highest contact rate in the youngest age- nd Bentley et al (1954) go so far as to say that is an inverse relationship between age and history tant contact

## Bronchoscopy

workers agree that as a therapeutic measure, scopy has not often been a success, and only rt (Margolisowa 1953) could be found in which sion occurred in most cases There are a few indications however and these include (1) collapse particularly involving the lower lobes spected suppurative lesion distal to bronchial ion (Bentley et al 1954) (3) obstructive ma (perhaps as an emergency procedure) and bly stridor The advisability of bronchoscopy esence of stridor is debatable because cases have been seen where the added œdema following the bronchoscopy has been sufficient to turn a partial obstruction into a severe and dangerous one

In segmental lesions associated with primary tuberculosis bronchoscopy may well come to be used more as a diagnostic than a therapeutic weapon With the increasing use of B C G bronchoscopies may become more often necessary to establish the nature and cause of a radiological lesion in a vaccinated child The decisions regarding therapy may thus be made easier though attempts to obtain either pus or granulation tissue will it seems, succeed in only half the cases

The findings in 44 children subjected to bronchoscopy are presented in table V These children all had a primary complex with some collapse or consolidation and in 12 children bronchoscopy was repeated more than once (on four occasions in 1 child) in an attempt to clear an obstructed airway 11 of the children were aged less than 2 years and several less than 1 year yet *they presented no great technical difficulty* Various combinations of pulmonary collapse were discovered usually only one lobe was affected in particular the right upper lobe Collapse of the right middle and lower lobes was the most usual combination seen Endoscopy revealed tuberculous granulations from rupture of a gland through a bronchus in about half the cases (20 out of 44) Such granulations were always removed at operation but subsequent bronchoscopy a few months later often showed that granulations had formed again Other endoscopic findings of primary importance were bronchial narrowing from external pressure of glands (4 cases) ulceration (1 case) pus exuding from a bronchus (2 cases) and a scarred stenotic bronchus (2 cases) No abnormality was detected in 15 cases the obstruction causing the collapse being apparently beyond endosco

TABLE V—BRONCHOSCOPY FINDINGS AND EFFECTS IN 44 CASES

| Findings | Improved | | No improvement | |
|---|---|---|---|---|
| | Primary importance | Secondary importance | Primary importance | Secondary importance |
| Granulations | 0 | | 11 | |
| Associated obstructive emphysema | | 4 | | |
| Associated stridor | | [illegible] | | |
| Narrowing from pressure outside bronchus | 1 | 3 | 3 | |
| Bronchial stenosis | | | 2 | 3 |
| Bronchial ulceration | | 1 | 1 | |
| Pus in lumen | | | 2 | 2 |
| No abnormality found | 1 | | 14 | |
| Total | 11 | 10 | 33 | 5 |

TABLE VI—INCIDENCE OF STREPTOMYCIN THERAPY AMONG 477 CHILDREN WHO SURVIVED

| Primary lesion | Age (yr ) | | | | | | | | | Total | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | $0–2^{11}/_{12}$ | | | $3–5^{11}/_{12}$ | | | 6–12 | | | | | |
| | Treated | Not treated | Total | Treated | Not treated | Total | Treated | Not treated | Total | Treated | Not treated | Total |
| ry complex | 15 | 111 | [illegible] | 6 | 132 | 13 | 4 | 115 | 119 | 21<br>(6* ) | 353 | [illegible] |
| on and " flare "<br>mination | 4 | [illegible] | 6 | 3 | 6 | 9 | 7 | 1 | 6 | 14 | 0 | [illegible] |
| | 1 | 1 | [illegible] | 3 | 5 | 6 | 0 | 11 | 11 | 1 | [illegible] | [illegible] |
| s meningitis | 5 | 0 | 5 | 10 | 0 | 10 | 4 | 0 | 4 | 19 | 0 | 19 |
| erculosis and meningitis | 4 | 0 | 4 | 1 | 0 | 1 | 4 | 0 | 4 | 9 | 0 | 9 |
| liary tuberculosis | 11 | 0 | 11 | 7 | 11<br>(1 unknown) | 6 | 4 | 0 | 4 | 2* | 11 | [illegible] |
| otal | 40<br>(26 ) | 114 | [illegible] | [illegible]<br>(16 ) | 1141 | 173 | [illegible]<br>(15 ) | [illegible] | 130 | 92<br>(19* ) | 1385 | [illegible] |

Including tuberculous mastoiditis and bone tuberculosis pic view, or else these may have been examples of periglandular "flare"

No particular age group derived greater benefit from bronchoscopy than any other, so the group is taken as a whole Immediate improvement was apparent in only 11, in whom removal of granulations allowed rapid re-expansion of the collapsed lobe (9 cases) or stridor to diminish considerably (2 cases) In the other 33 cases endoscopy produced no permanent change in the local condition, and re expansion of the lung took its time The deduction is that bronchoscopy can be undertaken in a child with a primary complex and pulmonary collapse in the hope of clearing the affected bronchus from caseous infective material and improving the airway Except for occasional immediate postoperative œdema with distress the procedure was harmless It must be admitted, however, that on rare occasions the postoperative condition gives some cause for uneasiness In only 1 case did further collapse occur after endoscopy

### Treatment

The general plan included hospital treatment during the very active stage and, as soon as possible, transfer to the country branch of Great Ormond Street, other convalescent institutions, or home, according to the progress and domestic circumstances of the patient When circumstances permitted, the children were treated entirely as outpatients (Hall 1951) Sanatoria specifically designated for tuberculosis were used only in exceptional cases, usually in children with parenchymatous lung lesions and cavitation Nearly all were subsequently followed in the tuberculosis clinic at Great Ormond Street or medical outpatient department at University College Hospital

Streptomycin, *p* aminosalicylic acid, and, more recently, isoniazid have been used in selected cases only Almost all (49 out of 55) the children with serious forms of tuberculosis who were admitted to hospital and subsequently died were treated with one or other or a combination of these drugs

Analysis of 477 of those who survived (table VI) showed that 19% were thus treated, those with miliary tuberculosis and tuberculous meningitis invariably and those with local dissemination almost always In dealing with a primary complex, with or without collapse and consolidation, specific therapy was given only in 6%, mostly for those with questionable spread to the surrounding parenchyma and with other complications, such as bone tuberculosis and mastoiditis irrespective of the age of the child Only 15 of the 126 children with this lesion and aged less than 3 years were given antibiotic therapy, and 11 of these were aged less than 1 year Limiting the treatment in this way runs rather counter to the ideas of many present day pædiatricians (e g, Todd 1952, Wallgren 1950), and particularly the French (e g, Debré 1951, Cathala et al 1949) who advise giving specific antibiotics to all children aged less than 1 or even 2 years with a primary complex Although the tendency now is to give all infants antibiotic treatment, the previous policy, which is adopted also by Dufourt et al (1950) and Miller (1952), seems fairly well justified when the prognosis is studied Critics might argue that more cases of miliary tuberculosis and meningitis might have been avoided if streptomycin had been used as a routine, especially in the younger children Some workers—e g, de Beule (1952) and Lorber (1950)—make the point that there is no certainty that such treatment will prevent these complications, which may even arise during therapy (Sacrez and Burghard 1951) and have done so in a very few cases in the present series The course the lesion took was usually most satisfactory, re aeration of the lung proceeded steadily, and healing took place with calcification Although the use of antibiotics in [illegible] ng lesions is undisputed, there is no evidence in the present series that they have any caseating adenitis or an associated pulmonary or that they will hasten recovery This cond accordance with the findings of Russell and (1950) and Lorber (1950)

### Lobectomy

There is little doubt that, with the passage thoracic surgery will play a more extensive treatment of tuberculosis in children The for surgery, the best stage of the disease at apply it, and the relative merits of hilar segmental or lobar resection are all subjects of Excellent results have followed lobectomy in 7 present series The children were aged 1–10 tion and 6 of the 7 had previously been bronch without benefit Only 2 children received and *p* aminosalicylic acid to cover the operation this is now standard practice They all did were discharged from hospital from ten to days after operation It is considered the operation is not indicated, and these cases for surgery because the child's general con poor and there was no evidence of healing of lesion over some years The 1 exception was aged 7 months who was not progressing after five months' observation but did very right mid and lower lobectomy at the age The endoscopy findings included granulations, ulceration, and scarring, and the lobectomy revealed collapse, bronchiectasis, caseation, cation

### Prognosis

Of the 215 surviving children who have been up from two to five years only 1 child died after the onset of the illness The outlook who have survived 2 years is good and a fair of immediate prognosis can therefore be made follow-up of this duration Most of the chil in fact, been under supervision far longer shows the clinical and radiological state when was discharged or when last seen in 1953

Of the 215 children 152 were well clinically logically, 47 were in good health but had radiological shadows (the lobectomy cases are in one or other of these groups) Only 4 were and were radiologically abnormal In ad children were under observation for non-tu conditions or because of residual complicati tuberculous meningitis Experience has resolution of the segmental lesion takes about whatever the cause, though the radiological take rather longer to clear in the younger chil

TABLE VII—PROGNOSIS IN 215 SURVIVORS

| Length of follow up (yr) | Clinically and radiological well | | | Clinically well with persistent radiological lesion | | | Ill with radiological lesion | | |
|---|---|---|---|---|---|---|---|---|---|
| | Age at onset (yr) | | | | | | | | |
| | 0–2 11/12 | 3–5 11/12 | 6–12 | 0–2 11/12 | 3–5 11/12 | 6–12 | 0–2 11/12 | 3–5 11/12 | 6 |
| 2 | 12 | 11 | 22 | 5 | 5 | 5 | (1) | | (1) |
| 3 | 13 | 17 | 14 | 4 | 5 | 2 | 2 | | |
| 4 | 11 | 14 | 8 | 5 | 4 | 3 | 1 | (1) | (1 |
| 5 + | 11 | 12 | 7 | 6 | 1 | 2 | (1) | (°) | 1 |
| Total | 152 | | | 47 | | | 4 + ([illegible]) | | |

The numbers in parentheses indicate the age (yr) lobectomy was done Since these children are now they have been included elsewhere in the table re exclude the fatal cases considered below, the liate prognosis (2–5 years) in this series is universally Even in the 13 survivors who had pleural effusion itlook seems good only 1 showing symptomless ogical abnormality within this limited period Of survivors who had local dissemination 7 did well the 12 survivors who had miliary tuberculosis all vivors who had tuberculous meningitis and all 6 iad both did well Of the 30 survivors without ications only 3 had symptomless radiological s Many of the children were left with areas of ation either in the primary focus or in the hilar or scattered in the lung fields Increasing density calcification was observed as the years passed and sumed to be good evidence of healing Later in children the area involved diminished and some calcium appeared to be absorbed

## Deaths

exact estimation of mortality in a condition with a natural history as tuberculosis is difficult The ng figures are of value only as an estimate of the five year death rate and the longer follow up will nuch greater interest It is realised also that there mavoidable selection of cases and that the over all rate is higher than it would be in entirely unselected of primary tuberculosis. The fact that some of the were *treated in the early days of streptomycin* y also has some bearing on the figures They vell be of interest however to those who work in als with a similar intake of patients to that at ospital for Sick Children and University College al.

ong the 578 patients who had active primary nary tuberculosis 58 (9 5%) died, and the lowest rate of the two hospitals was 8 7% The main found *post mortem* are given in table VIII table includes 3 cases of non pulmonary primary ulosis which were added for interest )

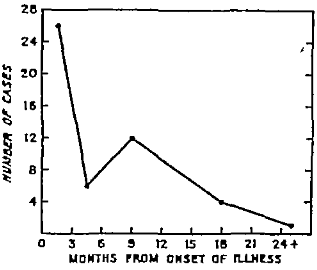
one might expect the commonest lesion was ulous meningitis with or without miliary tubercu nd this was most often observed in the younger n Tuberculous bronchopneumonia and extensive ing lesions accounted for most of the remaining For the purposes of comparison the lesions found pulmonary tuberculosis have been included and clusion of these and of those cases in which mary site was unknown does not significantly the mortality rate which was 70 out of 665 )

0 of the 55 deaths the duration of the tuberculosis be assessed accurately and the findings are shown accompanying figure Over half (26) died during st three months and a further 18 within the first There were only 5 deaths after that and only 1 lied after two years had elapsed This indicates as regards the immediate mortality a two year up is probably adequate in most cases disregarding later deaths from reinfection or reactivation tuberculosis

VIII—MAIN LESIONS FOUND POST MORTEM IN 58 CASES

| Lesion | Age at onset (yr ) | | |
|---|---|---|---|
| | 0–2 | 3–5 | 6–12 |
| ulous meningitis | 9 | 5 | 0 |
| ulous meningitis and miliary culosis | 15 | 10 | 4 |
| tuberculosis | 4 | 0 | 1 |
| ital lesions | 8 | 3 | 1 |
| dissemination and broncho monia | 7 | 1 | 0 |
| lmonary tuberculosis with or ut miliary tuberculosis and ngitis | 5 | 2 | 2 |

All except 8 cases had antibiotic treatment



Time of death in 49 cases

Table II shows the relative frequency of death from tuberculous meningitis and miliary tuberculosis alone and in combination. This includes cases with non pulmonary primary foci giving a total of 57 It shows at a glance that the presence of miliary tuberculosis in cases of tuberculous meningitis weighs *heavily against the chances of survival* In the younger age-groups 73% and 79% of children with the combined lesion died whereas only 58% and 32% of those with meningitis alone died Even in the children aged 6–12 years this striking difference is evident Miliary tuberculosis by itself however seems to be less fatal than meningitis but once again the younger the patient the worse is the prognosis. These conditions were fatal in 60% of the 55 children aged less than 3 years and in 35% of the 20 children aged 6–12 years.

With advances in antibiotic treatment the mortality rate should diminish With more immediate examination of contacts and early diagnosis it is hoped that these figures will be greatly reduced There is in fact, some evidence of improvement already

## Conclusions and Summary

The complications source of infection and bacteriology in cases of primary tuberculous complex of the lung have been studied The part played in their treatment by streptomycin and other specific antibiotics broncho scopy and lobectomy has been reviewed and the prognosis and mortality have been assessed

This study confirms once again the relatively good short term prognosis of the pulmonary primary complex in childhood The mortality rate of less than 10% in this rather selected series of cases compares favourably with the results of other units and would, of course, be reduced if the ' non active ' cases were included It might be argued that the number of cases developing serious complications, and therefore the mortality rate would have been lower if streptomycin and other specific antibiotics had been used more often

It seems unlikely that the unusually high incidence of segmental lesions observed in this series is due to this factor it arises through unavoidable selection of the more serious cases the classification used and the individual variation in terminology and interpretation of the radiological segmental lesion A follow up for two to five years has shown that most of these lesions resolve within two years.

The extremely low incidence (4 2%) of proved bronchiectasis following such lesions is explained by the fact that the resulting bronchial dilatation is usually symptomless and does not impair general health Usually bronchography was done only in cases with persistent ill health and abnormal clinical findings therefore proof of the presence of these symptomless lesions (which seem to be of little importance) is wanting

The presence of miliary dissemination in cases of tuberculous meningitis weighs heavily against the chances of survival and these two complications of the primary complex remain the principle dangers. This review includes the early streptomycin era, it is therefore hoped that future series treated with this and the newer antibiotics, alone or in combination, will have a lower mortality. The value of streptomycin and *p*-aminosalicylic acid in these cases has been obvious, yet in this survey 60% of children aged less than 3 years, of whom practically all received this treatment, died from these conditions. A plea is made for early diagnosis and institution of treatment, and examination of all contacts, particularly of children aged less than 3 years.

Although bronchoscopy has been of some value in diagnosis, and with the increasing use of B C G will probably become more so, its use in treatment is very limited. Greatest benefit has been derived in cases with stridor and obstructive emphysema, and most workers agree that these findings justify bronchoscopy. Opinions vary about the other indications for bronchoscopy, but these probably should include massive persistent collapse, particularly of the lower lobes.

Lobectomy is undoubtedly well borne by children, and one is impressed by the short time it takes them to become fully active after the operation. Although some workers advocate early surgical intervention, it is the opinion of most that lobectomy should be reserved for cases which have not responded to a reasonable period of adequate medical treatment.

I am greatly indebted to Dr B E Schlesinger for the clinical details of his cases from University College Hospital and the Hospital for Sick Children, to Dr Marcia Hall for the clinical records of the cases attending the tuberculosis clinic, and to both for their invaluable help and kindly encouragement in the production of this paper. I thank the physicians at the Hospital for Sick Children for granting access to the records of cases in their charge, Mr James Crooks, Mr H S Sharp, and Mr D J Waterston for their bronchoscopy reports, Prof R S Pilcher and Mr Waterston for the lobectomies, Dr Martin Bodian and staff for necropsy and biopsy reports, Dr I A B Cathie and staff for the bacteriological findings, Dr L G Blair and staff for radiological reports and advice, all the housemen and registrars whose notes made this report possible, and the chest physicians of various clinics for forwarding follow up reports.

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# INITIAL CONTROL OF HYPER WITH PENTOLINIUM TARTRAT

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ALTHOUGH a completely satisfactory treat essential hypertension has yet to be devised, re have produced a surfeit of hypotensive drugs, many are no better than a placebo, but some— hexamethonium and pentolinium tartrate—have their worth sufficiently to supplant sympathec a treatment of choice

In the Gateshead group of hospitals methon have been used from the autumn of 1950, and to their effect more completely a clinic for hyp started in the summer of 1951. From Octob pentolinium tartrate ('Ansolysen') was used subsequently most of the new patients with hyp were treated with this drug in preference to At present the patients who were receiving methonium with a retarding agent by daily sub injection are being given pentolinium tartrate by

The results of this policy will take some years to we report here merely the method used for st patients on pentolinium tartrate in hospital.

## Type of Patient Selected

Up to now 72 hypertensives have been ad hospital for treatment with pentolinium tartrat method of selection was similar to that of M (1952). We recognise the following groups:

(1) Labile hypertensives, with diastolic pressure be mm Hg but no complications, who require only reassurance, and reduction of obesity.

(2) Patients with persistent hypertension (diastolic 120 mm Hg or higher) and established complicatio

(3) Patients with malignant and premalignant hy

Most of the patients treated with pentolinium t were in groups 2 and 3. They had persistent diastolic blood pressure or persistent symptoms headache, breathlessness, dizziness, and failur Nevertheless, if severe symptoms were present, with diastolic pressure as low as 100 mm H treated.

## Symptoms and Signs

The following symptoms were present in the 7 at the time of selection for treatment:

Headache
Feeling of fullness in head
Dyspnœa
Vertigo
Angina pectoris
Fainting
Palpitations
Paræsthesiæ of extremities
Noises in head
Dependent œdema
Epistaxes
Failing memory
Loss of concentration
Failing sight due to hypertensive retinopathy

The age and pathological distributions were as

| *Age* (*yr*) | Male |
|---|---|
| 20–30 | 1 |
| 31–40 | 1 |
| 41–50 | 5 |
| 51–60 | 3 |
| 61–70 | 4 |
| 71–80 | 8 |

| ogical distribution | | |
|---|---|---|
| ign essential | 11 | 41 |
| gnant | 1 | 5 |
| al | 0 | 1 |
| locrine | 0 | 0 |
| rosclerotic | 1 | 8 |
| ertension following toxaemia of pregnancy | | 1 |

re were 59 females and 13 males Most of the its were in the 6th decade

### ocardiographic Changes

the 72 patients 47 showed electrocardiographic es amounting usually to those associated with left icular preponderance and axis-deviation 28 of these lso inverted T waves and S–T segment abnormalities t ventricular strain. 1 patient with associated ysema and cor pulmonale had right axis deviation

### graphic Changes

patients showed appreciable enlargement of the entricle and massive cardiac enlargement was it in 2.

### l Changes

70 patients whose fundi were visible fundal changes present as follows grade 4 in 5 grade 3 in 8 rade 2 in 35 Grade 1 changes in the vessels were t in 9, and there were none demonstrable in 13

## Contra indications

se patients were not admitted until 1000 calories d weight reduction had been given a thorough trial ue A history of angina pectoris, coronary throm or cerebral thrombosis was not regarded as contra ting treatment with pentolinium tartrate and mild ion did not prevent its use Senile dements were ed A raised systolic blood pressure with arterio us was not treated unless accompanied by per ly raised diastolic pressure

do not intend to discuss the effects of pentolinium te on renal blood flow Tests of renal function f limited character A raised blood urea level or paired urea clearance previous nephrectomy or s kidney disorder was a signal for circumspection rising blood urea level led to discontinuation of ent Patients with malignant fundal changes reated despite a rising blood urea level. The single assified as renal hypertension was one of only mild ephrosis, with normal renal function and this t has so far done well However since this series mpleted a rapidly rising blood urea level has been ed during treatment of 1 patient who had had s nephrectomy for hydronephrosis

ents with prostatic symptoms intestinal distension oma should not be treated

## Procedure in Hospital

patients were re examined on arrival and uro tests urea-clearance tests, intravenous pyelo- chest radiography and electrocardiography were Piperoxane or phentolamine tests were given to d patients Of 72 patients only 1 was found to nilateral renal disease on routine pyelography and ubtful whether this procedure is necessary when ne is chemically and microscopically normal The l pulses of all patients admitted were examined the present 72 and the 185 followed in the clinic pertensives no case of coarctation of the aorta o our notice

### Observations

often stated (e g Ronnov-Jessen 1954) that the should have a preliminary eight to fourteen days ital to allow the blood pressure to reach a resting Though we admit the desirability of a control we are doubtful whether it is economically to give such periods of up to a fortnight to s who may occupy a quarter of the beds in the hospital wards In place of this one can rely on preliminary outpatient observations coupled with a known history of hypertension and a relatively short period of up patient observation in hospital followed by a control day of two hourly blood pressure readings It is not important to know whether the patient s blood pressure will come down to near normal with rest in bed in hospital nor is it essential to give from three to five days rest in hospital before observations are made on blood pressure response to hypotensive drugs The problem is not the patient in hospital but the patient in home office or workshop Comparative freedom from the constant irritations and worries of domestic and working life make hospital surroundings artificial and lessen the value of blood pressure readings taken there Ideally blood pressure observations should be made in kitchens offices workshops, and factories The alternative in a medical ward is the encouragement of activity Patients were therefore kept up between 8 A.M and 8 P M and required to walk twice the length of the ward before recordings were taken

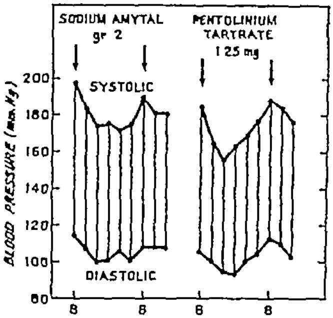

Fig 1—Comparison of effects of sodium amytal gr 2 and subcutaneous pentolinium tartrate 1 25 mg given at 8 a.m. and 8 p.m (averages of blood pressures of 12 patients)

Morning blood pressures may be rendered abnormally low by the use of barbiturate sedatives which were therefore not given during the period of hospital assessment The effect of Sodium amytal' on the blood pressures of 12 patients is compared with that of pentolinium tartrate in fig 1

### Day before Trial Dose

Control observations were made on the blood pressure every two hours from 8 A.M until midnight In the case of known hypertensives of some years standing this

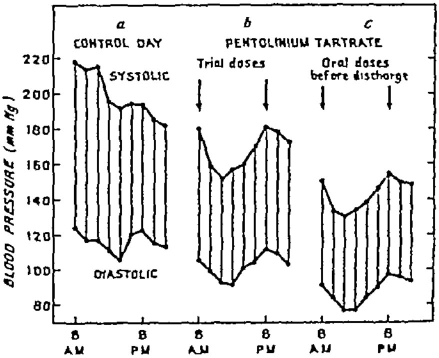

Fig 2—Average blood-pressure readings of 12 hypertensives two-hourly from 8 a.m. to midnight. Average time between b and c is ten days.

could be done on the first day Admittedly the morning blood pressure tended to fall spontaneously on subsequent days but the effect of pentolinium tartrate could be assessed by the shape of the two hourly curve without reference to the day to day fall

Fig 2*a* shows the average results of two hourly blood-pressure controls in 12 hypertensives who were up between 8 A M and 8 P M and in bed subsequently The day time blood pressures were observed after brisk walks along the ward It will be seen that the blood-pressure had dropped by 2 P M and reached a day-time minimum at 4 P M This fall took place in 9 of the 12 patients from whom the average blood pressure curves are constructed in the figure After 4 P M the blood-pressure rose again, reaching a peak when the patients received their visitors between 7 and 7 45 P M, and fell after their return to bed at 8 P M Lights were extinguished at 10 P M

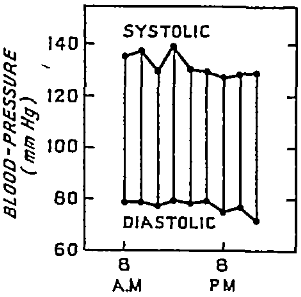

**Fig 3—Average blood-pressure readings of 12 normotensives two-hourly between 8 a.m and midnight. Compare fig 2*a* and note absence of fall of diastolic blood pressure at 4 p m and smaller fall between 10 p m and midnight.**

The importance of this control is manifold It establishes that the hypertension is persistent throughout the day, and it serves as a base from which the effects of hypotensive agents can be estimated Were this control to be omitted, the 4 P M fall might be attributed incorrectly to the effect of pentolinium tartrate The diurnal variations of blood-pressure may serve as a guide to variations in the dosage of the hypotensive drug

Fig 3 shows the corresponding two hourly control blood-pressures taken in normotensives The fall at 2 P M is no longer seen, the fall at 4 P M is very much less, and the blood-pressure varies much less than in hypertensives (fig 2*a*)

## *Day of Trial Dose*

On the following day a subcutaneous trial dose of pentolinium tartrate was given The makers recommend a trial dose of 2 5 mg but this occasionally alarming falls in blood pressure, therefore all the patients were given a trial dose of 1 25 mg Ev comparatively small dose led to diastolic blood of 50 mm Hg and associated faintness requir venous methylamphetamine in 3 patients, 1 of severely shocked, sweating, and pale

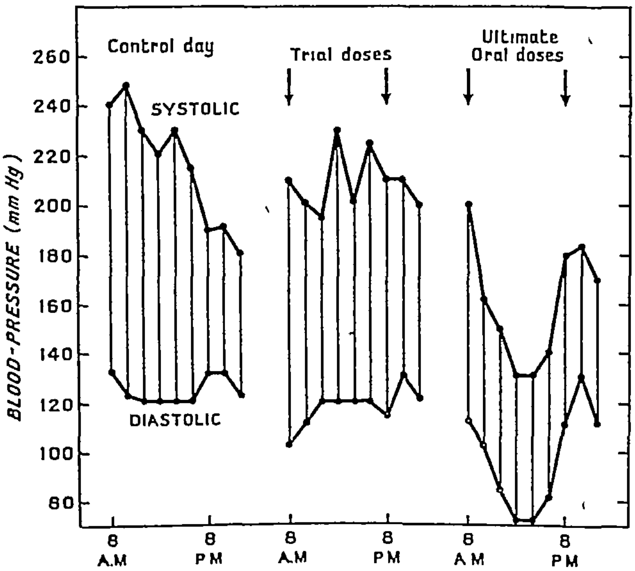

**Fig 4—Two-hourly blood-pressure readings in a patient who gave no response to trial doses of pentolinium tartrate 1 25 mg subcutaneously Note subsequent response to twelve-hourly dosage ( curve indicates that eight hourly dosage would be better)**

This trial dose was given solely to detect reactions In 15 patients the blood pressure did appreciably after the trial dose, but such response was not regarded as contra indicat treatment (fig 4) In 12 of these 15 patients not respond to their trial dose the blood successfully reduced in hospital

2 patients had unexpected falls in blood pre in the treatment 1 was a moderate fall on the day, the other was a more dramatic fall on t teenth day (fig 5)

Fig 2*b* shows the average blood pressure of h tensives given a trial dose of pentolinium tartra 8 A M 1 25 mg was given The maximal effect noon, and some was still present at 2 P M, but it was wearing off by 4 P M The blood-pressure sometimes regained the previous levels between 6 P.M and 8 P M if no further dose was given

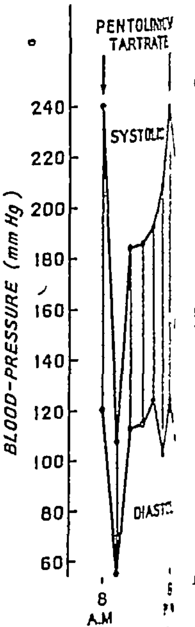

**Fig 5—Excessive fall pressure on nineteenth treatment with tartrate.**

## *Subsequent Days*

The trial dose was repeated on the evening of the first day, on the second day the dose was increased to 2 5 mg, and thereafter daily increments were made until the diastolic blood pressure reached 80 mm Hg The dose can be given either twelve hourly at 8 A M and 8 P M, eight-hourly at 7 A M, 3 P M, and 11 P M, or seven hourly at 7 A M, 2 P M, and 9 P M The shape of the curve produced by the subcutaneous trial dose should help one to select the proper interval between doses, but the individual convenience of the patient must be considered

We usually reduced the diastolic pressure to Hg by subcutaneous injections before changing tablets, 40 mg of oral pentolinium tartrate being lent to 2 5 mg of subcutaneous pentolinium This policy was dictated by the considerati patients might require such high dosage of pen tartrate as to render oral preparations unsafe, tating a reversion to the subcutaneous route happened in only 1 case of malignant hyperten oral preparation is now being successfully earlier at one hospital, where sometimes only the dose is given subcutaneously Pentolinium tartr usually much better tolerated by mouth than cutaneous injection, and, when excessive giddiness or hypotension followed subcutaneous a change to the oral route was usually all th necessary

With oral pentolinium tartrate the dose was by 20 mg (half a tablet) each day until the blood-pressure fell to 80 mm Hg and remain for at least two readings on both of two success

TABLE I—IMPROVEMENT

| Symptom | Present on admission (no of cases) | Still present but improved (no of cases) | Complete relief (no of cases) |
|---|---|---|---|
| e | 47 | 26 (55%) | 14 (30%) |
| f fullness in head | 25 | 16 (64%) | 3 (12%) |
|  | 56 | 32 (57%) | 1 (2%) |
|  | 51 | 26 (50%) | 14 (28%) |
| ectoris | 34 | 22 (64%) | 6 (18%) |
|  | 25 | 3 (12%) | 16 (64%) |
| ons | 41 | 21 (51%) | 11 (27%) |
| ske of extremities | 23 | 9 (39%) | 5 (22%) |
| head | 25 | 9 (36%) | 9 (36%) |
| nt oedema | 25 | 8 (32%) | 10 (40%) |
| s | 12 | 0 | 11 (92%) |
| emory | 27 | 11 (40%) | 3 (11%) |
| oncentration | 28 | 12 (43%) | 6 (21%) |
| ight due to hyperten tinopathy | 42 | 13 (31%) | 3 (7%) |

on the patient was discharged This process m four to twenty six days (average ten days) rage dosage when the patient left hospital was by mouth The largest twice daily dosage was and the largest thrice daily dosage 220 mg

## Immediate Results of Treatment

*n of Blood pressure in Hospital*

reductions of blood pressure in up patients in were as follows

*Diastolic blood pressure (mm Hg)*

| *Initial* |  | *On leaving hospital* |
|---|---|---|
| 1 | < 50 | 1 |
| 5 | 51–70 | 6 |
| 0 | 71–80 | 38 |
| 5 | 81–90 | 16 |
| 7 | 91–100 | 5 |
| 19 | 101–110 | 5 |
| 11 |  |  |
| 17 | Total | 71 |
| 6 |  |  |
| Total 71 |  |  |

g the course of hospital stabilisation 1 patient n cerebral hæmorrhage

e 26 patients whose diastolic pressure was not to 80 mm Hg most were disharged for such social as responsibility for children in the home business or a previously booked holiday In es of patients we reduced the diastolic pressures nm Hg in most of the non malignant hyper

I shows the improvement in symptoms from twelve months after discharge It will be seen melioration of the major symptoms of hyper headache breathlessness and giddiness is in three-quarters of the cases Angina sometimes l as a contra indication of treatment was helped The most striking result concerned repeated which did not recur in 11 out of 12 patients l up to twelve months Compared with other series, improvement of vision was a disappointment although in the early stages of treatment of malignant hypertension it was occasionally remarkable

LE II—SIDE EFFECTS OF PENTOLINIUM TARTRATE

| effect | No of cases | Subsequent improvement (no of cases) | Remedy |
|---|---|---|---|
|  | 0 | 0 | Treatment discontinued |
| ion | 11 (15%) | 0 | Simple laxatives cholinergic drugs |
|  | 0 | 0 | Chalk mixtures |
| outh and a | 26 (36%) | 13 | Pilocarpine nitrate gr 1/5 neostigmine 15 mg |
|  | 0 | 0 |  |
| of urine | 0 | 0 | Urecholine |
| sion due to s of accom on | 14 (19%) |  | Eserine drops in eyes, change of spectacles |
| lls of blood | 5 (7%) | 5 | Methylamphetamine |

*Side-effects*

With dosages of either 220 mg three times a day or 280 mg twice a day severe reactions such as paralytic ileus and retention of urine, were not observed Larger doses were not used, because we felt that ileus might follow their use Table II shows the side effects observed in the 72 patients treated

Most of the patients tolerated dryness of the mouth without undue complaint the remainder were helped by pilocarpine It was not usually necessary to instil eserine drops into the eyes Where paralysis of accommodation made reading difficult patients had their spectacles changed as soon as a reasonably constant dosage was reached

## Aftercare

Within three weeks from their discharge from hospital all the patients were seen at the clinic for hypertensives when their progress was reviewed and dosage changed if necessary

Very few patients maintained the lower levels of blood pressure after discharge from hospital therefore the dosage of pentolinium tartrate almost invariably had to be increased Symptomatic relief, however, persisted

Some of these patients have now been followed for twelve months During this time 2 of them have died of cerebral hæmorrhage (1 had ceased to attend the clinic) and 1 who had malignant hypertension has died of pulmonary embolism complicating left and right ventricular failure

## Conclusions and Summary

After three years experience of the treatment of hypertension in hospital and in a clinic for hypertensives a method of initial stabilisation of patients on pentolinium tartrate has been evolved

The method requires that patients shall be up during the greater part of the hospital day and be exercised before blood pressure estimations which are taken sitting erect two hourly

The initiation in general practice of hypotensive treatment with pentolinium tartrate is inadvisable because of the liability to occasional severe reactions which need prompt counter measures

Pentolinium tartrate is rapidly superseding hexamethonium retard as the hypotensive agent of choice

In essential hypertension and in a few cases of malignant hypertension it is possible to reduce a patient's diastolic blood pressure from almost any level to 80 mm Hg for three or four hours out of twelve on several successive days before the patient leaves hospital

It has not usually been possible to maintain the blood pressure at this level after the patient has left hospital Nevertheless blood pressure levels achieved with hexamethonium and other drugs can be equalled and symptomatic relief is the rule

Preliminary two hourly blood pressure readings are important in deciding the subsequent treatment

After the midday meal there is in ambulant patients a natural drop in the blood pressure which might be mistaken for a therapeutic effect if these control blood pressure readings were not taken

The trial dose of pentolinium tartrate should be only half that at present advised by the makers

Failure to obtain a response to a trial dose should not deter one from treating with pentolinium tartrate because a bigger dose usually produces a satisfactory response

Our grateful thanks are due to Dr C N Armstrong for permission to include cases admitted into his care at the

Queen Elizabeth Hospital, Gateshead, and to Dr H A Dewar, who first encouraged the use of pentolinium tartrate in place of hexamethonium in the hospital group and has advised us constantly since

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# "EPIDEMIC VERTIGO" WITH OCULOMOTOR COMPLICATION

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A GENERAL practitioner requiring assistance with a patient who has suddenly developed vertigo is likely to find the choice of consultant a little embarrassing Shall he burn his boats and summon a neurologist or an otorhinologist or more cautiously turn to a general physician as a neutral referee ? Ultimately each of these specialists sees his fair share of such cases, and from his individual experience each would probably be able to recollect an occasional example of the mysterious malady usually referred to in this country as "acute labyrinthitis"

Perhaps on account of its sporadic occurrence and benign character, the condition does not seem to have attracted much attention until the appearance of an annotation in *The Lancet* (1952) This suggested that there might recently have been a small epidemic of this disease and cited the experience of a Hampstead doctor who had had 6 cases in his practice during January, 1952 In the subsequent brief correspondence only two general practitioners (Currie 1952 and Fry 1952) claimed to have had a similar experience in the immediately preceding months , but later Burrowes (1952) described elsewhere 6 cases of this type seen in a general practice during the same period. Several other writers indicated that they were familiar with the condition and in particular Worster-Drought (1952) contributed an authoritative account based on records of almost 50 cases seen in neurological practice over a period of seven years The features which he considered characteristic were vertigo of sudden onset with vomiting and nystagmus, though this last feature was by no means always present Coördination appeared never to be affected, and there was rarely significant deafness though some patients described transient tinnitus Recovery was the rule, though this might take from six weeks to twelve months and in the early stages relapses were common Worster-Drought emphasised that "acute labyrinthitis" (a designation which he accepted) could be diagnosed only after other causes of vertigo had been excluded, and that in this connection the absence of persistent deafness and tinnitus was strong evidence against Ménière's syndrome

More recently Dalsgaard-Nielsen (1953) has summarised a study of 21 cases of "epidemic vertigo" admitted to hospital in Copenhagen within the past few years These cases he considered were representatives of an epidemic which had been prevailing in Denmark generally The chief interest of this paper lies in the additional features which were occasionally observed, for in its essentials the clinical picture seems to have been identical with that seen previously in this country 2 of the patients, for example had diplopia, and one or two more had unequal pupils Hiccup was a complication on 2 occasions, and 6 of the 13 cases studied by electro encephalography were said to show dysrhythmia Although the cerebrospinal fluid (C S F ) was invariably found to be normal Dalsgaard-Nielsen concluded that there was every justification for regarding this condition as encephalitis

My first encounter with this rather alarming found me singularly unprepared Indeed had it my good fortune to see in rapid succession of almost identical character, I would remained unenlightened Some of the cases in the outbreak, however, presented features which appear to have been described in this country

## Case-reports

**Case 1** —A fitter, aged 54, seen in consultation 1954, had been perfectly well until ten days previously on return from a football match he was suddenly intense vertigo At the same time he began to vomit ing persisted for three days, and he remained in any change of posture caused renewed vertigo after the onset, following a bout of vomiting diplopia which persisted and did not vary with ment At the same time he was aware of transient tinnitus in the right ear, but he had not noticed any He had had no headache or other symptoms, and afebrile He had had no previous illnesses of

*On examination* his general condition was good, comfortable while lying supine , change of posture vertigo, though this was less severe than previously cardiovascular system was normal , blood pressure Hg with no palpable thickening of arteries abdomen were normal There was no neck optic discs were clear , there were no retinal changes reactions were normal , eye movements appeared there was no nystagmus, but diplopia was present the range of eye movement , there was no cranial nerves were otherwise normal There was no tremor or other evidence of incoördination of arms tendon reflexes were brisk and equal , power and of all limbs were normal , the abdominal present , the plantar responses were flexor Urine

The diagnosis at this time appeared uncertain thought that a small brain stem thrombosis might these developments After a further week, since little improvement in his condition, he was Doncaster Gate Hospital, Rotherham, for lumbar and further study

*Investigations* —The C S F , which was under normal and was clear, contained 14 red blood-cells and cytes per c mm and protein 70 mg , sugar 82 mg 738 mg per 100 ml , the Lange gold curve was and the Wassermann reaction and Kahn test were The erythrocyte sedimentation rate was 9 mm in the (Westergren) , blood count normal. Radiographs and chest were normal. An ear, nose, and throat could find no aural abnormality, but an reported that the diplopia was due to paresis of superior rectus

*Treatment and Progress* —The patient was treated low salt diet, and continued mild sedation. improved and left hospital after a six week stay weeks after the onset he was still troubled by slight postural dizziness

**Case 2** —A girl student, aged 19, admitted to Infirmary, Sheffield, on Oct 5, 1954, had been until two days previously when unusually for late, failing to hear her own alarm clock and two She was aroused with some difficulty and noticed On getting out of bed she tended to stagger to the there was no true vertigo Twenty four hours developed occipital headache and vomited remained drowsy throughout the day At this doctor could find no neurological signs When hospital the following morning she was already she was bright and cheerful and free from headache and diplopia, though she described at first some focusing objects

*Examination* —On admission her temperature and pulse rate 100, but within twenty four hours normal Routine clinical examination was negative pressure 120/45 mm. Hg Urine normal There rigidity, and Kernig's sign was negative , pupil normal, and there was no nystagmus , to ordinary movements were full although occasional e was observed (full ophthalmic examination a day ater revealed no ocular paresis); optic discs clear ess No incoördination or paresis of limbs tendon minal reflexes normal and plantar responses flexor; unimpaired. On lumbar puncture the C.S.F. pressure ult to record but appeared lower than normal The s clear and contained no excess of cells; the protein was 30 mg and sugar 65 mg per 100 ml. the Lange ve was normal. White blood-cells numbered 5000 with normal differential count.

ss was uneventful and the patient returned to ing-college after a week's stay in hospital by which was free of symptoms She has remained well since gnosis again was in doubt: mild encephalitis was to be a possibility but disseminated sclerosis could gether be excluded.

3.—A poultry farmer aged 27 admitted to the firmary Sheffield on Oct 20 1954 had been very until six days before admission when he had been seized with vertigo while going to bed The vertigo he remained in bed and the following night was vomiting During the next few days he improved and did not again vomit but on the day before n the vertigo was more pronounced and his doctor lely dilated inactive pupils. There was no complaint che or diplopia, but there was occasional tinnitus ght ear

*ation.*—On admission his general condition was good vas afebrile Routine clinical examination was nega lood pressure 132/64 mm. Hg Urine normal There neck rigidity and Kernig's sign was negative pupils l size and active optic discs clear eye movements but pronounced rotary nystagmus was present ed by extension of the head and on looking to the ere was no deafness or evidence of local ear disease tion of the central nervous system otherwise revealed rmality power and coördination of limbs was , abdominal and tendon reflexes were normal and ar responses were flexor and sensation was unim On lumbar puncture the C.S.F., which was clear and ormal pressure contained 1 cell per c.mm and 0 mg and sugar 55 mg per 100 ml Lange gold as normal White blood-cells numbered 8000 per th a normal differential count

*s.*—There was at first little improvement in the nd once sudden vomiting without warning followed of retro-orbital headache Anti histamine drugs to bring some relief and after a week nystagmus ed and recovery was well established and after in hospital the patient returned home When seen later he reported himself fully recovered apart from y to slight postural dizziness

—A shop assistant aged 25 seen in consultation 22 1954 had been well until three days previously he evening she had occipital headache and felt slightly hile at work the next morning she developed without cute vertigo and felt sick but did not vomit Return with difficulty she went to bed where the vertigo on any change of posture but she did not notice The following morning she complained of diplopia some left-sided retro-orbital headache but the as considerably improved

*mination* her general condition was good and she greatly distressed There was no fever Routine amination was negative; blood pressure 140/85 mm urine was normal There was no neck rigidity and sign was negative; both pupils were widely dilated ed only very slightly to light and on accommoda ere was evident paresis of the left internal rectus d gross rotary nystagmus on lateral eye movement tinct to the right; optic discs and retinæ were there was no deafness or other abnormality of erves Power and coördination of limbs were l; tendon and abdominal reflexes were normal plantar responses were flexor; and sensation was al.

*tions.*—The patient was admitted the next day aster Gate Hospital Rotherham, where lumbar yielded clear C.S.F. under normal pressure this no excess of cells the protein content was 30 mg ml. and other constituents were normal White s numbered 6200 per c.mm. with normal differential count An ophthalmologist confirmed the paresis of the left internal rectus and in addition drew attention to the presence of slight left-sided ptosis and paresis of the left inferior oblique muscle

*Progress.*—The patient recovered rapidly and within a further twenty four hours was free from vertigo nausea, and diplopia. At the end of a week she was discharged from hospital free of symptoms and with complete recovery of eye movements When seen a fortnight later she had no complaints.

**Case 5.**—A married woman aged 53 seen in consultation on Oct 23 1954 had been in excellent health until two days previously when while sitting in a friend's house she was suddenly attacked by acute vertigo accompanied by vomiting She was helped home and had remained in bed since lying very still because any change of position brought renewed vertigo She had not vomited again but noticed tinnitus in the left ear There was no diplopia but photophobia was quite pronounced Headache had not been a feature

*On examination* her general condition was good and routine examination was negative she was afebrile blood pressure 103/70 mm. Hg The urine was normal There was no neck rigidity and Kernig's sign was negative pupils were normal and optic discs clear eye movements were full but coarse nystagmus occurred on looking to the right. There was no deafness and cranial nerves otherwise were normal There was no loss of limb coördination and power abdominal reflexes were present and tendon reflexes were unaltered

*Investigations.*—The patient was admitted the same day to Doncaster Gate Hospital, Rotherham where lumbar puncture yielded clear C.S.F. under normal pressure containing no excess of cells and protein 55 mg per 100 ml; the Lange gold curve was negative. White blood-cells numbered 4600 per c.mm. with normal differential count

*Treatment and Progress.*—Despite treatment with a low salt diet and anti histamine drugs the subjective vertigo was slow in clearing but nystagmus persisted for only twenty four hours after admission. The patient returned home largely recovered after twelve days in hospital and when seen a fortnight later was complaining only of slight dizziness

## Discussion

The use of the term outbreak for a series of 5 cases may seem a little portentous, but there is some evidence to justify this description In the first place with clinical features so remarkably similar it can scarcely be doubted that each of these patients had the same disease and although a span of six weeks separated the appearance of the first and last cases the last 3 cases were seen virtually on successive days Lively expectations of an epidemic were not realised and as far as can be discovered there has not been a single further case All of the patients came from one locality living either in or within a few miles of Rotherham and during the same period no similar case appears to have been seen by consultant colleagues among the adjacent and much larger population of Sheffield It has been impossible to trace any connection or common source of contact among these 5 patients each of whom came from an entirely different walk of life

Fundamentally these cases conform exactly to the pattern noted previously Thus the patients were apparently all in excellent health up to the time of onset and in 3 the onset was dramatically sudden Invariably the initial symptom was vertigo or at least severe giddiness followed rapidly by vomiting of cerebral type or nausea None had ear disease or deafness, but 3 noticed transient tinnitus Nystagmus was observed in 3 cases; in 2 of these it was of rotary and labyrinthine type intensified by extension of the head but in no case was there any loss of coördination

The single feature which seems to distinguish this outbreak from any previously reported in this country is the occurrence of diplopia. Of the patients in this series 3 had diplopia and in 2 of these undoubted ocular pareses were observed. There is a strong probability that a 4th patient (case 3) also had involvement of the oculomotor nerve for dilated inactive pupil wer noticed by his doctor at one stage, and these were also observed in one of the patients (case 4) with external ocular pareses In the account of the Danish outbreak (Dalsgaard-Nielsen 1953) diplopia or pupil changes are mentioned in not more than 3 or 4 of the 21 cases reported, in comparison therefore the incidence of these complications in this small outbreak has been much higher

Obviously it should be more widely known that oculomotor control may also be disturbed in this condition, for without this information the diagnosis, at least in isolated cases, is bound to cause difficulty and probably some anxiety It follows also, in view of the wider neural involvement shown by these cases, that the description "acute labyrinthitis" is no longer acceptable On the other hand, in view particularly of the consistent failure to demonstrate any excess of cells in the C S F, some may find the concept of this disease as a "form of encephalitis" equally difficult to support At present, therefore, any description had best be non-committal, and for this reason the title "epidemic vertigo" has here been preferred

### Summary

A small outbreak of the disease usually referred to in this country as "acute labyrinthitis" is described.

This outbreak was confined strictly to one locality, but no source of common contact could be identified

An unusual feature was the high incidence of oculomotor disturbance—a complication, observed occasionally in a recent Danish epidemic, which has apparently not hitherto been reported in this country

It is suggested that until more is known of the ætiology of this disease the title "epidemic vertigo" is preferable to "acute labyrinthitis"

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# THE HAIR OF THE PILONIDAL SINUS

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SINCE Warren (1854) first described the pilonidal sinus a century of speculation has not finally decided its mode of origin Various developmental theories have been put forward from time to time (Hodges 1880, Wendelstadt 1885, Herrmann and Tourneux 1887, Bland-Sutton 1922, Oehlecker 1926) The embryology of the sacral region has been under more recent review (Kunitomo 1918, Kooistra 1942) The view of Patey and Scarff (1946, 1948) that the pilonidal sinus is essentially traumatic emphasises the weak foundations on which the developmentalist theories are based

In the present study the hair in the pilonidal sinuses was examined to determine its origin The premises were these

(1) If the sinus is a developmental anomaly, the hair should be growing out towards the skin surface in a more or less orderly fashion

(2) If the pilonidal sinus is the result of a mechanism such as was suggested by Patey and Scarff (1946), hairs found in the sinus should be lying at random in relation to the axis of the sinus

### Methods and Materials

Seven sacral pilonidal sinuses removed at were subjected to serial section The sections, 15 μ thick, were stained with Heidenhain's 'Azan' to demonstrate the structure of the hair cuticle

Direction of hair growth can be deduced from the direction in which the cuticular scales lie In practice, if hairs are cut obliquely and appear as oval discs, and if infection blurs the cuticular outline, difficulty may be experienced in deciding which way a hair has been growing The following criteria are then helpful

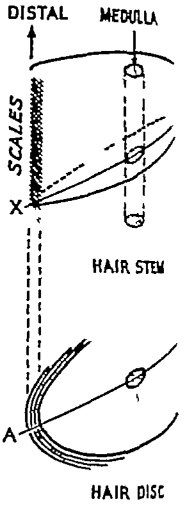

Fig 1—Oblique section (A hair stem cuts more mal end (A) than at hair segment. The more closely packed the

(1) The medulla is usually nearer the proximal extremity of the hair disc (fig 1)

(2) The basal edges of individual hair scales appear more closely packed than their distal cusps The former are smooth, the latter ragged.

(3) More dye tends to concentrate over the pro *of the hair disc*

(4) Owing to capillary attraction a dark band found just distal to the cusp of a scale, but as overlap the proximal scale is just a shade darker distal one

### Findings

The parallel course of many hairs suggest must originate in a fairly circumscribed are followed to their source (see above), apparent that they originate in the depths of Their deep ends are club shaped They in the lumen of the sinus, or they may still to the sinus wall (fig 2) In the uninfected points of attachment may show par may extend along the sinus wall

If it is accepted that the fine lanugo like hair hair (the club-like expansions make this virtual, all that should remain of the follicles is their External root sheaths may be seen soon after been extruded, the intercellular cement characteristically sloping into the lumen of away from the root base The internal root for a time, stick to the extruded hair Later remains as pale loose debris

Two kinds of epithelial linings are seen highly keratinised, and rich in rete pegs narrow, pale, and practically devoid of rete predominates in infected sinuses, and secon from islands of the thick original epithel inflammation has subsided

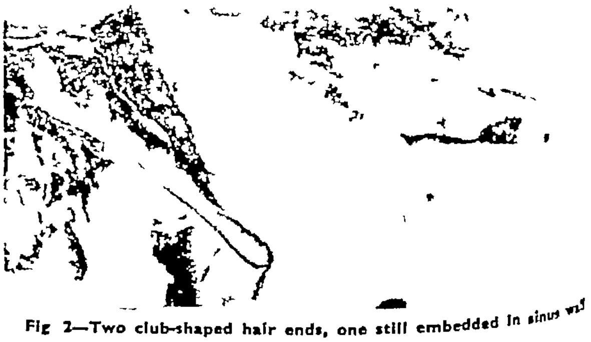

Fig 2—Two club-shaped hair ends, one still embedded in sinus wa

d inflammation become chronic masses of tion tissue are formed, encroaching on the lumen nus, burying the epithelium and finally absorbing ) With the epithelium hair particles are similarly in the granulation tissue but being unabsorb ey retain their histological identity They can e found some millimetres outside the chronic yet they betray their origin by the common n of their scales

kin overlying the sacral pilonidal sinus contains ly deep hair papillæ In a formol preserved erefore shrunk specimen they may be up to deep well in the subcutaneous fat The follicles separate from the sinus may be abnormally id carry two hairs each None of these features ionstrable in the sacral skin of normal controls is probable that they are an expression of the evelopmental anomaly which leads to the fully sinus They may be the precursors of undeveloped

### Discussion

ng developmentalists the precise mode of forma the pilonidal sinus is undecided The disparity n tail development and the cephalad movements pinal cord and skin introduces so many confusing that the segmental orientation of the sacral difficult to assess Though pilonidal sinuses are nes associated with other sacral developmental it is well to remember that such defects often n crops a causal relationship between one and is impossible to prove

findings on tracing the origin of the hair to the the pilonidal sinus provide evidence that this is elopmental defect The notorious absence of pillæ is no bar to such a view when the hair within us is recognised as shed.' Indeed the case with hair can be teased out of a sinus in the living would make any other finding surprising

Granulation tissue entering lumen of sinus and absorbing squamous lining (× 50)

### Summary

d section of pilonidal sinuses has demonstrated eir contained hair originates in their depth, and o sinuses are therefore developmental defects

r infection hair may penetrate the sinus wall and o lie outside the sinus Independent hair papillæ skin close to a sinus have been found to reach an l depth.

I wish to thank Dr A. D Morgan for his help and advice and Mr F E Wilson and Mr M Cuthbertson for their help with the histological preparations.

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# CEREBROSPINAL FLUID IN CARCINOMATOSIS OF THE MENINGES

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Cerebrospinal fluid (C.S F) containing little sugar and much protein and many cells is often regarded as pathognomonic of tuberculous meningitis. That carcinomatosis of the meninges can produce a similar picture has only recently been recognised (McCormack et al 1953) Apart from Forster (1930) and Platt (1951) who referred to the occasional recognition of tumour cells in the C.S F and Jacobs and Richland (1951) and Strange (1952) who reported low sugar levels few workers have correlated the presence in the C.S.F of neoplastic cells much protein and little sugar with the necropsy findings The similarity to tuberculous meningitis is illustrated by the following case

A man aged 64 was admitted to Seacroft Hospital on June 20 1954 with the diagnosis of tuberculous meningitis He had had pain in his trunk and limbs for twelve weeks this had become worse gradually in the last month when he had lost much weight and had developed pain and stiffness in his neck Thirteen days before admission he had a generalised convulsion with a period of unconsciousness. In the past he had been a miner and was in receipt of a pension from the Silicosis Board

*On examination* he was pale and wasted with a very stiff neck and a positive Kernig's sign His cranial nerves were not affected, his optic fundi were normal and there were no choroidal tubercles. His right lung showed emphysema with crepitations in the upper zone

*Investigations*—Radiography on July 1 showed pneumoconiosis with parenchymal infiltration of the upper zone of the right lung

Lumbar puncture on July 1 produced C.S F containing lymphocytes 100 per c.mm., sugar 20 mg per 100 ml protein 130 mg per 100 ml and chloride 570 mg per 100 ml

*Diagnosis and Treatment*—In view of the history the clinical state and the above-mentioned findings tuberculous meningitis was tentatively diagnosed Systemic chemotherapy and daily intrathecal therapy with streptomycin was begun Repeated lumbar punctures showed a persistently raised cell count much protein and little sugar (as little as 13 mg per 100 ml ) Cytological examination showed clumping of the cells on at least one occasion.

*Outcome*—The patient died in coma with anuria and jaundice twenty three days after admission

*Necropsy* revealed carcinoma of the stomach with metastases in the leptomeninges liver suprarenal glands, and lungs with associated silicosis, bronchitis, and emphysema. There was no tuberculosis. The meningeal involvement was confined mostly to the region of the basilar artery and the anterior surface of both cerebellar lobes. It was obvious on microscopy only to the naked eye it would have passed as a healing tuberculous meningitis. The rest of the brain appeared normal

These necropsy findings are exactly similar to those of McCormack et al (1953), who attribute the low C S F sugar level to the large demands of the active neoplastic cells for glucose

Carcinomatosis can only be distinguished from tuberculosis by finding malignant cells in the C S F This distinction is of importance because the recognition of carcinomatosis saves the patient from the rigours of intrathecal antituberculous therapy

My thanks are due to Dr E C Benn, consultant physician, Seacroft Hospital, for permission to publish, and to Dr W Goldie, consultant pathologist, for the necropsy findings

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# RETROSPONDYLOLISTHESIS AS A CAUSE OF PARAPLEGIA

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Retrospondylolisthesis in the dorsilumbar region of the spine is a well recognised clinical entity which causes local pain in the back and referred pain in the lateral aspect of the buttock There is often an associated degenerative arthritis of the hip-joint, this may make it difficult to determine whether pain in the region of the hip joint is due to primary disease of the hips or is referred from the spine

It is, however, unusual for retrospondylolisthesis to cause serious pressure symptoms and I have not been able to find any report in the literature of actual paraplegia being produced, so it seems worth reporting the following case Since treating this patient I have seen two further cases of retrospondylolisthesis with slight spasticity of the legs and it is possible th degrees of this condition are not uncommon

A married woman of 66, who was admitted to h April 20, 1954, had had pain in the lumbar region f years, and pain in the left hip for six years, with pr disability During the last two years she had bee walk only with assistance and inside the house, with k knees flexed For the last two years she had had inte urinary incontinence One week before admission t pital the pain in the left hip became worse and she b bedridden Her general health until recently had be but the pain had lately kept her awake and she h considerable amount of weight

She was a thin, rather querulous woman Both t knees were flexed to 90° and fixed Both legs were The tendon reflexes were not elicited, but there were plantar responses on both sides There was no d impairment of sensation The arms and cranial ner normal X ray examination showed retrospondyl of D12 and L1 Cervical myelography showed a complete block at the D12–L1 level (Lumbar my was attempted but was unsuccessful owing to ossif ligaments in the lumbar spine )

On April 27, 1954, laminectomy of D11, D12, and L performed The dura mater was found to be co at D12–L1, after laminectomy the constriction and normal pulsation returned below the level of th A fine rubber catheter could be passed up and down th without resistance

Postoperative progress was slow but steady from the day after operation Pain and cramp dis Spasticity gradually abated and urinary control Flexion deformities of the knees and hips had to be but she was ultimately discharged from hospital in Se walking unaided and only slightly spastic

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# Preliminary Communications

## STIMULATION OF NATURAL IMMU TO ESCHERICHIA COLI INFECTIO

### OBSERVATIONS ON MICE

It has been recently shown[1] that differe virulence of *Escherichia coli* strains for mice correlated in vitro with the survival rate of the in the presence of mouse serum and complem this bactericidal system the avirulent strains were killed under conditions permitting 100% survival virulent organisms

During attempts to isolate the bacterial subst this reaction, a remarkable effect of the bac walls came to light After injection of 0 05–0 2 *Esch coli* cell walls, either intraperitoneally ( intravenously (I V), mice showed greatly susceptibility to *Esch coli* infection if challenged i 2 hours but greatly reduced susceptibility if the c was delayed for 24 hours This initial decrease resistance, followed in 24 hours by a great in believed to be due to the rapid neutralisation *Esch coli* cell walls of the normally effective serum mechanism, which within 24 hours is restored to level than normal

EXPERIMENTAL

*Preparation of Cell Envelopes*—Strains of *Esch Salmonella typhimurium* were used

They were harvested in saline from 24 hours nutrient agar The suspensions were heated at 60 C min and then centrifuged, washed and suspended to an approximate dry weight of 30 mg bacteria 10 ml of this suspension was shaken in the Mickle together with 5 ml of ballotini beads for 40 min[2] T beads and any intact bacteria were removed by centr for 20 min at 3000 r p m in an M S E minor angle ce The turbid supernatant was further centrifuged at

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1 Rowley, D *Brit J exp Path* 1954, 35 (In the pres
2 Few, A. V, Cooper, P D, Rowley D *Nature* Lo 169 283

| alls<br>oli<br>ose | Time before challenge | No of organisms in challenge dose | Mice dead within 48 hr | |
|---|---|---|---|---|
| | | | Treated | Controls |
| I.P | 30 min | 5000 *Esch coli* 2380 | 2/3 | 0/3 |
| | | 500 | 3/3 | 0/3 |
| | | 50 | 1/3 | 0/3 |
| | | 5 | 2/3 | 0/3 |
| I.P | 48 hours | $2 \times 10^{8}$ *Esch coli* $V_6$ | 0/6 | 3/3 |
| | | $2 \times 10^{6}$ | 0/6 | 3/3 |
| | | $2 \times 10^{4}$ | 0/6 | 3/3 |
| I.P | 48 hours | × 10 | 1/9 | 3/3 |
| | | $2 \times 10^{3}$ | 0/5 | 5 |
| | | $2 \times 10^{4}$ | 0/5 | 5/5 |
| | | $2 \times 10^{6}$ | 0/2 | 2 |
| I.V | 48 hours | $2 \times 10^{8}$ *Esch coli* V | 1/3 | 3/3 |
| | | $2 \times 10^{6}$ | 0/3 | 3/3 |
| | | 2 × 10 | 0/3 | 3/3 |
| | | $2 \times 10^{3}$ | 0/3 | 2/3 |

alues in normal mice results V 10 organisms
pproximately 100 mice for V 10
strain 2380 10

hese columns numerators indicate numbers of death
nominators indicate total mice tested

in a Serval high speed angle centrifuge for 1 hour deposited the bacterial cell walls These were suspended M disodium hydrogen phosphate and treated with w/w pure trypsin under toluene for 7 days, after which soluble material was deposited by centrifugation and d once with saline and once with distilled water before dried from the frozen state

*ulence tests* of *Esch coli* strains were carried out as hed previously[1] by I.P injection of dilutions of hallenge culture suspended in 1 75% hog gastric + 0 4% charcoal.

*alls* —The table shows the effect of injecting various ities of cell walls prepared from *Esch coli* 2380 on survival of mice after challenge with three virulent s of *Esch coli* It will be seen that 30 minutes injection with the cell walls of *Esch coli* 2380 may be killed by as few as 5 *Esch coli* whereas 0 organisms are required to kill a similar proportion rmal mice On the other hand 48 hours after ion mice challenged in the same way may survive al thousand times the dose lethal for normal mice is effect is non specific among *Esch coli* strains it t associated with any rise in the serum agglutinin against *Esch coli* and there is no increase in the of complement The immunity is at a maximum 2 after injection of the cell walls and has fallen to the al level about 5 days later The protection can be vely transferred by the serum of one mouse to her

e cell walls prepared from antigenically unrelated ent or avirulent *Esch coli* strains or from various s of *S typhimurium* all produce the same effects rying degree. Hence either a specific factor respon for this effect is widely distributed in the coliform almonella families or else similar factors occur in the ent members of these two bacterial species The *coli* factor is extremely heat stable biological ity being little impaired by boiling for 7 hours

hen 1 ml of unheated guineapig serum was treated 0 5 mg of *Esch coli* cell walls, at 37°C the comple titre was reduced from 60 hæmolytic units to and this decrease was shown to be due to the dis arance presumably by adsorption of the $C_3$ fraction mplement This pheuomenon is analogous to the val of the $C_3$ fraction when serum is treated with the t polysaccharide zymosan [2] In fact injection ice with zymosan will exactly reproduce the effects d here with *Esch coli* cell walls Moreover rats h are normally resistant to infection with *Esch coli* strains + mucin become susceptible soon after I P injection of approximately 50 mg of zymosan Thus six rats when challenged after 30 minutes with 100 000 cells of *Esch coli* 2380 + 1 75% hog mucin were all obviously ill after 24 hours and two of them died six normal control rats appeared well and survived

DISCUSSION

Most animals are capable of removing enormous numbers of *Esch coli* from their tissues both by phago cytosis and by serum killing If the cellular defences are inhibited by the presence of mucin the serum is still extremely effective in killing most *Esch coli* strains There is apparently an efficient serum system capable of acting on some substrate in *Esch. coli* cells, and it is natural that in acting upon the organisms the chemical system in the serum—whether enzymic or not—will be attached to and temporarily removed by the bacteria If the bacterial substrate can be provided in some form other than living bacteria the serum system will probably be adsorbed by it and given the correct amounts the greater part of the serum killing system might perhaps be removed so that its efficiency in destroying viable *Esch coli* cells would be seriously impaired and the animal would become highly susceptible to infection

Pillemer et al[4] have shown that treatment of various animal sera with zymosan at 37°C not only removes the $C_3$ component of complement but also removes another immunity factor which they call properdin[5] They have produced evidence that the bactericidal action of fresh serum is due jointly to its complement and to its properdin content When animal species are arranged in a series according to the properdin content of their sera this order corresponds roughly with the level of natural immunity of the species. Thus rats show the highest and guineapigs the lowest properdin titres More recently Pillemer has shown that injection of mice or rats with either our *Esch coli* skin fraction or with zymosan following the procedure described here results in an immediate fall in the serum properdin level to about 20% of its normal value the level is then rapidly restored and after 48 hours may reach a value four times higher than the original normal level[6] This finding suggests that the initial fall and subsequent rise in the serum properdin level as demonstrated by Pillemer following injection of zymosan or *Esch coli* cell walls, may influence or be the direct cause of the changes in resistance of mice to *Esch coli* infection as found in the present experiments If so it means that in the mouse under the experimental conditions used the predominat ing defence mechanism against this infection must involve properdin and complement. Whether or not this mechanism plays a part in other infections has still to be determined We may, however note that Pillemer and his colleagues have found that injection of zymosan into mice or rats greatly decreases their susceptibility to the bacteræmia and death which follow irradiation of the whole body[7]

Sir Almroth Wright repeatedly spoke of a "negative phase" following inoculation of humans or animals with typhoid vaccine This negative phase was demonstrated by a decrease in the bactericidal power of the blood lasting up to several days according to the dose of vaccine employed Where a small dose was injected a great increase in the bactericidal power of the blood was occasionally noted within two days of injection[8]

I am grateful to Prof Louis Pillemer of Western Reserve University Ohio for a gift of zymosan and for providing unpublished data I am also indebted to my colleagues—to Dr P D Cooper for the preparation of some of the *Esch coli* cell walls to Dr D. Hobson for a supply of zymosan, and to Mr C R Jenkin for technical assistance

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[4] Pillemer L Blum L Lepow I H Ross O A Todd E W Wardlaw A C. Science 1954 120 279

[5] See Lancet 1954 ii 587

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## HYDROCORTISONE IN TREATMENT OF ALLERGIC CONJUNCTIVITIS, ALLERGIC RHINITIS, AND BRONCHIAL ASTHMA

HYDROCORTISONE has, in contrast to cortisone, a *local* effect in certain disorders of the skin and in arthritic joints We therefore thought it possible that it would have a beneficial local action on the mucous membrane in allergic disorders We briefly describe here the treatment with hydrocortisone of 4 patients with allergic conjunctivitis, 15 with allergic rhinitis, and 15 with bronchial asthma In all of these patients the disorder had been present for over a year, and in most for several years, and there had been little variation in the condition throughout the year—a factor which helped us greatly to assess the results

Hydrocortisone has only lately become available in this country In North America it has been found superior to cortisone in a number of cases of vernal catarrh,[1 2] and at least equal if not superior to, it in allergic conjunctivitis [3]

*Allergic Conjunctivitis*

Our 4 patients with typical allergic conjunctivitis, who had previously had local cortisone without success, were treated with daily instillations of hydrocortisone acetate (2 5 mg suspension in 1 ml physiological saline). 2 of these patients also had asthma and eczema, and were sensitive to various allergens For several years they had had continuous itching of the eyes and a viscous conjunctival secretion causing the eyelids to be glued together on waking The conjunctiva was slightly injected and had a milky œdematous appearance, particularly distinct in the lower fornix 2 drops (about 0 02 mg ) of the hydrocortisone suspension was instilled three times daily for two days

In the 1st case the symptoms disappeared completely for three weeks There was a recurrence after this time, and further treatment resulted in relief as before

In the 2nd case the symptoms were also relieved but recurred five days after cessation of treatment Continuous relief was achieved with a maintenance dose of 1 drop instilled every fifth day When an anti histamine drug was given by mouth at the same time this drop was required only every eighth or ninth day The conjunctivæ looked less red, but the milky œdematous appearance was still present

The 3rd patient, who showed the same signs but suffered only from excessive lacrimation, was treated in the same way and the day time lacrimation improved within forty-eight hours, after which there was negligible lacrimation at night

The 4th patient, whose allergic conjunctivitis was proved by the history and by conjunctival test to be due to cat fur, also improved under the treatment , but itching and redness did not disappear as in the first 2 patients

In the first 2 patients treatment was started with one eye only When there had been spectacular improvement of this eye both patients reported spontaneously that the other eye had also improved at the same time, but only partially

*Nasal Allergy*

The patients with nasal allergy had had rhinitis constantly for over a year All showed a typical swollen, boggy, mauve white, nasal mucosa In most cases the disorder was so severe that the use of decongestant drops could not be avoided , and in most local treatm zinc ionisation, cautery of the inferior turbinate, of polypi, or desensitisation had given no relief histamine drugs had, as usual, stopped running of the nose, but had left the swelling mucosa and therefore the blockage unchanged

These patients inhaled daily into their nos contents of a half or a whole celluloid capsule wi of hydrocortisone powder, from an Upjohn inhaler Every one or two weeks their nasal mu inspected A control period was obtained by the treatment for some weeks, or, in many case tuting an inert powder of similar taste for two weeks

In 11 of the 15 patients an important r improvement ensued They were able to breath through their noses and could either dispense a with nasal decongestants or limit their use to twenty four hours Shrinkage of the nasal was noted, but the boggy appearance and mauv persisted, except in 2 cases where the mucosa a normal in some places

In 1 of these it was thought likely that the norma of mucosa corresponded with those sites which w easily reached by the flow of the inhaled powd hydrocortisone was omitted the condition graduall ated in two to three weeks, but it improved two to th after treatment was resumed

In most cases treatment was started with on only, using the other as control , often the d obstruction was unequal, and the more severely nostril was selected for treatment first In th the improvement was sufficiently distinct to con previously " better " nostril into the " worse " t

In 4 patients the treatment was unsuccessful.

1 of these found the powder irritating to his nose and it In another patient a generalised urticarial rash within twenty four hours of the start of the treatme was abandoned Of the remaining 2 patients, 1 di the powder regularly

*Bronchial Asthma*

In the treatment of bronchial asthma the ch is the difficulty of depositing enough hydrocorti large surface area of bronchial mucosa It was to try inhalation of hydrocortisone powder with particle size of under 5 μ rather than inhalatio aerosol The amount of hydrocortisone powder through the mouth from a powder inhaler was or 7 5 mg per day

All 15 patients had perennial severe bronchial that demanded constant use of anti hist at bed time and of aminophylline or ephedrine the day In addition, to counter intercurrent spasm, they used an isoprenaline nebuliser 3- in the twenty-four hours Only those patien included whose condition had been stable for six months, and in whom the number of iso inhalations was approximately the same and this number was used to gauge the severity asthma After using hydrocortisone powder for three weeks these patients were given cartridge ing inert powder for the same period , after this them were changed back to hydrocortisone

In 11 patients the treatment caused definite ment of the asthma, the number of isoprenaline tions dropping to half or less When inert pow substituted the improvement persisted for up weeks, and when the asthma had returned to its severity resumption of hydrocortisone again relief An increase in the hydrocortisone dosage 15 mg per day did not cause further improveme

In 3 patients the treatment had no effect

The 15th patient had been on a maintenance dose of oral cortisone per day, and was using, in addition,

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[1] McDonald P R. Leopold I H. Vogel A W Mulberger R D *Arch Ophthal* N Y 1953, 49, 400
M. *Amer J Ophthal* 1954 37, 533
E H *J Amer med Ass* 1952 150 1660

no suppositories and 8–10 isoprenaline inhalations With this régime her condition did not vary for many hs When the 50 mg of oral cortisone were replaced mg of hydrocortisone powder a striking improvement red within two days. The number of inhalations dropped per twenty four hours and the aminophylline could be ed With 7 5 mg of hydrocortisone powder the condi was slightly worse than on 50 mg oral cortisone but 10 mg of hydrocortisone it was exactly the same and sage could be maintained at this level for many weeks

nce the systemic activity of hydrocortisone is at double that of cortisone[4] the effective equality mg of hydrocortisone powder with 50 mg of oral sone suggests a local action of the former In the majority of the cases hydrocortisone definitely oved the condition but did not completely abolish sthmatic obstruction

### DISCUSSION

r experience with local hydrocortisone in the ment of allergic eye nose and bronchial disorders o limited for definite conclusions about optimum ge and method of application and the type of patient likely to benefit most But we are sure that in these conditions it can be of therapeutic value Local treatment has the advantages that the need for large systemic doses of cortisone with the attendant dangers of systemic therapy, is avoided, and that it is more economical

We are indebted to the physicians of the chest department for access to their patients to Messrs Upjohn of England, Ltd for the supply of hydrocortisone powder and the powder inhaler and to Messrs Roussel Laboratories for the supply of hydrocortisone suspension One of us (H H.) was assisted by a personal grant from the Medical Research Council.

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Arbesman, C F., Richard N B J Allergy 1954 25 306

# Reviews of Books

## al Health and Human Relations in Industry

Editor T M LING M A D.M Oxfd M.R.C.P., medical director Roffey Park Institute of Occupational Health nd Social Medicine London H K Lewis. 1954 Pp 265 21s

DUSTRIALISATION which has brought profound ges in individual and group relationships, is thought rry with it a higher incidence of psychological and hosomatic disorders. High rates of absenteeism, strial fatigue and accidents and sickness and osis are it seems, an almost inevitable part of rn society but perhaps they were of any society Mayo, as long ago as 1924 showed that the level roduction and the morale of a group of factory ers correlated more highly with their sense of rtance and responsibility to the community than the hours worked or the level of pay Since then ation has been directed to the study of the interionships of men and groups rather than of the e worker Many recent researches suggest that mployee often feels dissatisfied because he has no of belonging to a group or because he has no s. He feels insecure and frustrated and cannot t himself to his surroundings. The most satis ry industry is one composed of small primary groups e interests correspond with those of the concern whole

Ling has edited a collection of essays, by authorities ndustrial research and psychology dealing with al health in industry from many different aspects. imself suggests that wages and security prestige approval and the value and creativeness of the itself as well as the sense of belonging to a group eeds which must all be satisfied to ensure the mental h of industrial workers. In meeting these needs medical officer the psychiatrist the personnel ger and representatives of industrial management interdependent rôles to play—rôles which are fully ssed by the various contributors. This is a useful informative book

## Vitamins

*hemistry Physiology Pathology* Vol. II Editors: H SEBRELL, jun director National Institutes of Health Bethesda Maryland; and ROBERT S HARRIS professor of biochemistry of nutrition Massachusetts Institute of Technology Cambridge New York: Academic Press. 1954 Pp 766 $16 50

IE second volume in this new series of reference works e vitamins deals, in turn with choline the vitamins ssential fatty acids inositols the vitamins K nicoacid and pantothenic acid It is closely modelled on the first volume[1] and like its predecessor owes much to successful coöperation between the editors and contributors Each section on each vitamin has been written by an expert, yet overlapping has been largely avoided Although the main emphasis is on the chemistry and physiology of the vitamins their occurrence in Nature their pharmacology and the effects of deficiency in man and animals are also discussed, and on the whole a comprehensive account is given of present knowledge If the third and final volume reaches an equally high standard the series should be a valuable source of well documented up to-date information Both volumes are well printed and illustrated and carry author and subject indexes

## Foundations of Surgery

GEORGE PERKINS, M.C., M CH F.R.C.S professor of surgery London University Edinburgh and London E. & S Livingstone 1954 Pp 230 10s

Surgery for Toddlers' is the alternative title which Professor Perkins, in his preface offers for his useful and amusing little book It is intended for the student who has just finished his anatomy and physiology and is starting in that mood of relaxation which follows a major examination his first year of clinical work. Here is a small agreeable guide to the country which lies ahead something which he can read (and which, thanks to its dignified title he can be seen reading) in the train something which points out the main roads and gives him the lie of the land without luring him into fascinating but bewildering byways. It is written in short, brisk and often amusing sentences and it is full of memorable and important facts. Nothing could be better designed for warding off the slothful habits natural as Professor Perkins remarks to most medical students.

## Treatment of Acute Poliomyelitis

2nd ed Editor WILLIAM A. SPENCER M D department of pediatrics, physiology and physical medicine Baylor University College of Medicine Springfield Ill: Charles C Thomas Oxford Blackwell Scientific Publications. 1954 Pp 134 27s 6d

THIS small book summarises a course of lectures on the treatment of acute poliomyelitis, delivered at the South western Poliomyelitis Respiratory Center Texas

The 23 contributors represent all specialties associated with the disease—with the exception of anæsthetics which has not yet come to play much part in the treatment of poliomyelitis in the U.S.A Hence there is no mention of positive pressure respiration through a cuffed tracheotomy tube There is much else to be learned from these pages however The reader gains an instructive insight into an American

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1 See Lancet 1954 ii 857

respiratory centre with all its functions, from nursing to biochemical studies There is a good account of glosso pharyngeal breathing by which the patient learns to force air down his trachea by a movement of his mouth and throat, pumping one mouthful after another into his lungs until they are well distended, and then breathing out Another interesting device is "the vacuum cleaner assisted cough" for respirator patients The positive end of a vacuum cleaner is led into the tank respirator in such a way that a positive pressure phase of up to 40 cm of water is reached The patient is taught to hold his breath as the pressure rises and then to cough at the highest pressure

Those who treat poliomyelitis will find in this book many such practical hints The first known record of a case of poliomyelitis—on an Egyptian plaque—adorns the cover

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**Neuro-Ophthalmology** (2nd ed Springfield, Ill Charles C Thomas Oxford Blackwell Scientific Publications 1954 Pp 591 £6 6s)—Prof Donald J Lyle's new edition is essentially a new book, about twice as long as the first, and containing some 100 more illustrations It has even been differently planned, the first half now relating many clinical anomalies to the anatomy of the eye and to the central and vascular connections of the globe, and the rest of the text being given to clinical entities with a rather broader basis Though the arrangement is not strictly logical, it has the merit of dealing adequately with clinical affections in terms of basic physiology and pathology The text is competent and the illustrations include many that are good, new, and distinctly original, though a few seem to lack point

**A Practical Manual of Diseases of the Chest** (4th ed London Oxford University Press 1954 Pp 647 84s)—Despite the great accumulation of new knowledge since the last edition, Dr Maurice Davidson and Dr John H have accomplished the task of revising this book minimum of important omissions and with some r in the number of pages A practical manual should only information that is fully substantiated and no versial, but the indications prescribed here for lung fall short of modern surgical practice, and the use of surely deserves more space than the effects of climat use of cortisone and of corticotrophin in sarcoid bronchial asthma has wisely been left for consid a later edition The book is carefully written and be produced

**Rötgenanatomische Grundlagen der Lunge suchung** (2nd ed Budapest Akadémiai Kiadó Pp 315 Ára 180)—This handsome and finely il volume from Hungary, compiled by Dr F Kovats, Dr Z Zsebök, is much better produced than any textbooks on radiology which have reached this It is to a large extent an atlas with cross sections and sections through the lungs related to the radiographs. The first chapters, on the anatomy bronchial tree and the segmental relationships, closely to Brock's work, which is suitably ackno The anatomy of the pulmonary vessels is worked angiography, but here there is not sufficient emphas wide intrapulmonary variations Identification of intrapulmonary structures by means of tomography attempted The best sections are those which show drawings the three dimensional levels of the bronchi an them to bronchograms All the line drawings and anatomical specimens, many of which are in excellent Many of the radiographs are poor, and not of the quality of the paper or printing Either the equipment or the film emulsion, or both, are inferior to

# New Inventions

## OROTRACHEAL CONNECTION WITH MINIMAL RESISTANCE

FIG 1 shows a new design in adult orotracheal connection intended for adults, to minimise resistance to breathing in clinical anæsthesia, and to reduce th intrathoracic pressure in patients with res paralysis due to poliomyelitis being treated with mittent positive-pressure respiration through endotracheal tube This reduction is achieved more rapid emptying of the lungs during the ex phase owing to absence of resistance

Fig 2 shows how a standard Magill endotrache is connected direct to the valve mount of a apparatus

Fig 3 illustrates how all the usual sources of have been removed, the lumen is gradually re kept smooth, and the size of the orifice is (actually 0 5 mm larger) to that of the tube it fits

The connections are made in three sizes, 8, 10, to fit tubes size 8 to 12 They are in two shapes with a 90° curve (fig 1*a*) for standard use, and a 135° curve (fig 1*b*) for operations about the he for poliomyelitis patients

The resistance to inspiration in these connect from a quarter to a tenth of that in common connections There is no measurable resista expiration, whereas in standard connections re expiration is much the same as that to inspiration

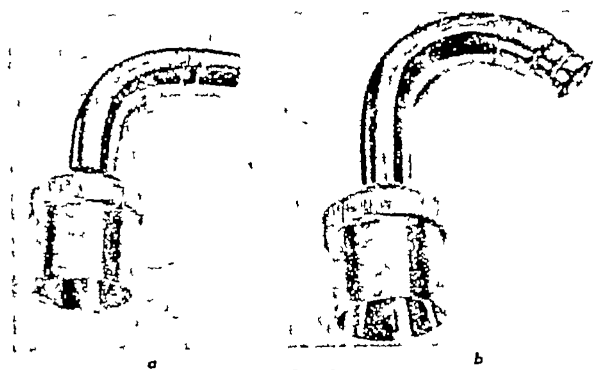
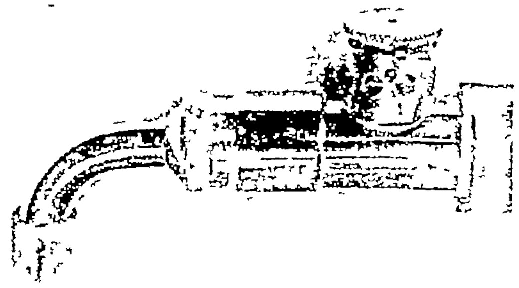


Fig 1



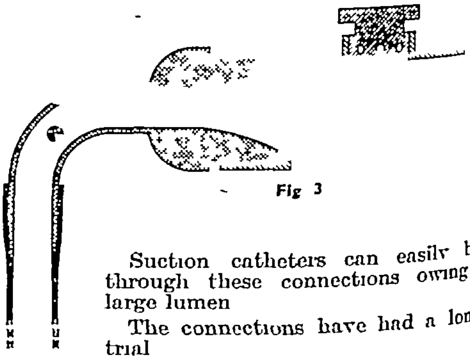


Fig 3

Suction catheters can easily be through these connections owing t large lumen

The connections have had a long trial

They are obtainable from Messrs Charles King L

Southern Hospital,
Dartford

JOHN BULLO
M B Lond, F F

# THE LANCET

*LONDON SATURDAY JAN 20 1956*

## Total Gastrectomy

mortality of total gastrectomy is falling Until was 54%[1], now Marshall and Uram[2] find is just over 8%, compared with 35% in the 1927–43 In this decline there is danger for ns may be tempted to do the operation more and like all amputations it is not to be under lightly The only real justification for excising ole stomach is in an attempt to remove growth

A benign ulcer high on the lesser curve may mes call for section through the œsophagus t total resection results but in these circum a gastric tube can usually be fashioned from ater curve or even the distal half of the stomach o pyloric canal Again when at laparotomy it rtain whether an ulcer is benign or malignant gastrectomy may be inevitable for frozen s at the time of operation give little help since o difficult to interpret and the specimen may een taken from an area free of malignant cells ubmitting a patient to total gastrectomy it must ne in mind that though he may not become a nvalid he will no longer be the man he was y suffer from dysphagia due either to a disturb f the hiatal pinchcock with consequent reflux gitis and even pharyngitis or (particularly if n is present) to deficiency of the vitamin B x which Brain and Stammers[3] found in 9 of patients they followed up Sooner or later kely to become anæmic One thing is certain fail to gain weight and strength and may deteriorate in both these respects It is now n knowledge that this is due to steatorrhœa s of nitrogen in the fæces Kelly and nsteen[4] have investigated experimentally the effects on absorption of different types of mosis In dogs they made pouches from n and these proved satisfactory reservoirs not stem the loss of weight or prolong survival ound that only œsophagoduodenal anastomosis llowed by longer survival Welbourn[5] has that the fat loss differs little whether the œsophagus is anastomosed to duodenum or to jejunum and this disposes of the idea that fat is lost entirely because the pancreatic juices chase food instead of mixing with it As regards nitrogen loss Johnson et al[6] report a considerable improvement when food is enabled to pass through the duodenum When, therefore after total gastrectomy it is possible to join the œsophagus to the duodenum this should probably be done All else that can be done is to modify the diet Brain and Stammers recommend fractional' fat feeding for they found that weight was gained on hourly feeds of small amounts, but Butler et al[7] on the other hand suggest that the steatorrhœa be treated with a diet high in protein and sugars and low in fats, in particular avoiding fats containing saturated long chain fatty acids

An operation which induces such sequelæ must have substantial advantages in other ways, and these have not yet been established for total gastrectomy The evidence indicates that for carcinoma of the stomach this operation has no greater effect on survival than partial gastrectomy Finsterer's[8] longest survivors had been treated by partial gastrectomy and so had those in the 1486 cases reviewed by Stammers[9] but these patients were mostly operated on at a time when total gastrectomy was less common From their statistical data Walters et al[10] concluded that provided that resection clears the primary lesion (and for this purpose total gastrectomy is not always necessary) any recurrence is usually not in what remains of the stomach, but in viscera adjacent to it and elsewhere within or behind the peritoneum Though pancreas and spleen are sometimes included in total gastrectomy it is impossible to excise the whole potential field of metastatic deposit Marshall and Uram[2] who have studied 202 patients with total gastrectomy, of whom 184 had malignant tumours have also come to the conclusion that total gastrectomy does not increase the proportion of five year survivors and they recommend that it should be done only in selected cases Nuboer[11] has shown that in cases of carcinoma of the cardia an operation which preserves the distal part of the stomach will give a 35% five year survival It therefore seems that there is only one indication for total gastrectomy—when the growth involves so much stomach that the primary lesion can be encompassed in no other way—and this holds whether the aim is cure or palliation Regarding survival the crux of the matter lies in the extent not of the operation but of the lesion. If, by luck the lesion is confined to the stomach there is a chance of eradication by partial or total gastrectomy If the neoplasm has spread beyond the stomach any excision is in the nature of closing the door after the horse has bolted Even extensive excisions which include much of the lymphatic field and the parietal peritoneum spleen and pancreas may not succeed for from the stomach with its copious blood and lymph supply metastases are likely to be carried in all directions once either stream is entered

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J M. T Rienoff W F *Arch Surg., Chicago*, 1929 10

all S F Uram H *Surg Gynec Obstet* 1954 99 63

R H F Stammers F A R. *Lancet*, 1951 i 1137

W D Wangensteen O H *Arch Surg Chicago* 1951 116.

urn R. B *Gastroenterologia Basel* 1954 81 109

[6] Johnson A Goldman L, Davi C Harper H., McCorkle H J., Gardner R. Surgical Forum Philadelphia 1953 p 40

[7] Butler T J Capper W M., Naish J M *Gastroenterologia Basel* 1954 81 101

[8] Finsterer H *Wien klin Wschr* 1947 59 17

[9] Stammers F A R *Proc R Soc Med* 1949 42 66

[10] Walters, W., Gray H K., Priestley J T *Proc Mayo Clin* 1952 27 136

[11] Nuboer J F *Proc R. Soc Med* 1954 47 109

# Isoniazid Resistance

ISONIAZID RESISTANT tubercle bacilli behave oddly Some do not grow in the usual culture-media, and many are apparently avirulent in guineapigs and mice Certain strains require in their environment substances that have catalase or catalase like activity Such strains themselves are deficient in catalase, and COHN et al[1] found that this deficiency is closely related to the attenuation of the strain Thus, strains completely catalase-negative were avirulent in guineapigs, while catalase-positive strains were only slightly or moderately attenuated MIDDLEBROOK et al[2] investigated the catalase activity of cultures obtained from patients before and during isoniazid treatment They found that almost all highly resistant strains were catalase-negative Some sputum specimens yielded cultures which were less resistant to isoniazid, and these contained catalase positive strains that were pathogenic to guineapigs Some cultures clearly consisted of mixtures of catalase-positive and catalase-negative strains Since catalase-positive resistant strains were not isolated from any patients in whom treatment had been begun with a daily dose of 8 mg isoniazid per kg body-weight, MIDDLEBROOK et al recommend that this dose should be adopted, on this scale the dose for a ten-stone patient would be 500 mg, which is much greater than that usually given in this country MIDDLEBROOK et al admit that there is no "unequivocal evidence" that catalase-deficient strains are attenuated in man In fact, there does not seem to be any such evidence at all Isoniazid-resistant bacilli seem capable of producing disease KATZ et al,[3] for instance, reported a case of rapidly fatal tuberculous pneumonia in which a culture before treatment contained strains resistant to isoniazid and streptomycin Treatment with both drugs failed to alter the course of the disease The strains, which were highly resistant to isoniazid in vitro, produced disease in guineapigs, their catalase activity was not determined

The Medical Research Council workers have investigated the results of sputum-culture and sensitivity tests six to nine months after treatment with isoniazid was discontinued[4] 43 patients had resistant strains when treatment was stopped after three months, and 20 of these still had positive cultures at the end of a year On the other hand, only 3 of 22 with sensitive cultures remained positive This does not suggest that patients with resistant strains in the sputum become culture-negative more rapidly than those with sensitive strains, as might possibly be expected if resistant strains were less pathogenic in the environment in which they originated The character of the disease was different in the two groups, the resistant group containing more patients with extensive cavitation Without collapse treatment or resection these would be less likely to become culture-negative, and it is not stated whether either of these measures was applied It has been reported that isoniazid-resistant strains tend to disappear from the sputum after treatment has been stopped, and hence that the cultures have a lower level of resistance or become fully sensitive The M R C report does no this Although there were some differences b the sensitivity of cultures at the end of treatm six or nine months later, there was no clear e of general reversion It is sometimes f cultures of tubercle bacilli are heterogeneous tions, and sensitivity tests may record the resistance of only the most highly resistan in an unknown critical proportion Thus the isolation of strains resistant to streptomycin, salicylic acid, and isoniazid from sputum d necessarily imply that all, or even the maj the bacilli in the culture are resistant Only small proportion may be resistant to each combination of drugs, and most may be to all For instance, in the case reported b although strains resistant to isoniazid and mycin singly were isolated, growth of the completely inhibited by low concentrations of drugs together To explore the drug a culture fully would require many more tests than are at present done routinely, it doubtful whether the information obtained w clinically important enough to justify the work, but fuller quantitative investigation bacillary populations in sputum and in the p lesions themselves would obviously be valu research, and improved laboratory methods to increase the clinical value The medium MIDDLEBROOK et al,[1 2 5] for instance, is cl reduce the delay in reporting and make it e primary isolation to estimate the propor bacilli of different degrees of sensitivity A containing charcoal, developed by HIRSCH, claimed to give quicker growth and to be prepare and sterilise than media containing albumin, but so far this has not been t primary isolation

The bacillary population in the patient's l probably even less uniform than that in the s and its constitution cannot be determined examining the excretion of the bronchial tr is the lung a simple culture medium The requirements of isoniazid-resistant bacilli in th may be different from those in the lab Bacteriological investigations are easier t out and simpler to interpret than clinical and there may be a tendency for bacteriolog to be too readily accepted as guides to tr DRESSLER and MIDDLEBROOK, and their colle Denver,[7] have treated a group of patien advanced pulmonary tuberculosis by brief bed rest and early graded activity in add isoniazid with or without streptomycin The no evidence that treatment in hospital with rest in bed adversely affected the patients treatment was based on the "conviction th azid holds a unique position"[7] and that "the tion of isoniazid resistant mutants of tuber for guineapigs and rabbits must have significance"[8] Although unsupported by co clinical evidence, these convictions demand for there is no firm evidence that isoniazid nce has a similar significance to streptomycin nce Isoniazid resistant bacilli as we have said

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[1] Cohn M L Kovitz C Oda U Middlebrook, G *Amer Rev Tuberc* 1954 70 641

[2] Middlebrook G, Cohn M L Schaeffer W B *Ibid* p 852

[3] Katz S, Storey P B McCormick G F *Ibid* p 881

[4] Medical Research Council no 6 *Thorax* 1954 9 254

[5] Cohn M L, Oda U Kovitz, C Middlebrook G *Tuberc* 1954 70 465

[6] Hirsch J G *Ibid* p 955

[7] Dressler S H Anthony E M Russell W F Denst J Cohn M L Middlebrook G *Ibid* p

[8] Middlebrook G, Dressler, S H *Ibid* p 1102.

## Slum Children Today

families of four or five live in one tenement room g the exhibits was a drawing of a bedroom little r than a cupboard, into which two double beds a cot could just be crowded ; here no less than eight ns slept, ranging in age from twenty years to or six

quotation from an editorial[1] on a London g exhibition in 1932, may be matched by one Miss Vera Poole s article on London slums in nchester Guardian of Nov 13, 1954

family of seven in three small rooms one room p entirely to the married daughter and husband remainder (six) sleep like sardines in two beds in er room "

verbal descriptions are reinforced by the figures Victor Freeman medical officer of health for on, in his annual report for 1953

ngton is not favoured with large open spaces and average of 76 2 persons per acre it is among the zen or so most densely populated boroughs in the of London no single ward can serve as a r other parts of the borough and in every ward the lon density exceeds the average for the County of 59% of nearly 82,000 Islington households o bath of their own and another 20% share a 53% of Islington households share even a water

ns that we have little to show for our twenty ears of slum-clearance and Prof Fraser ngton (p 244) explains how this has come Up to 1939 our schemes had resulted in the tion of a quarter of a million slum dwellings had all been replaced by better houses but ystem of exchange had unfortunately done g to reduce overcrowding Since then we have ny houses by enemy action and our population reased On the other hand thanks to much new g not associated with slum demolition we are first time getting abreast of the overcrowding n and even—taking the country as a whole— ing to get ahead of it. To increase this slight r even to hold it we shall (as he shows) have to ard and plan well

ne particular the picture has changed since 1932 se days all who lived in overcrowded squalid presumably did so from necessity , now Miss finds some do it from choice A single striking e from among several reported to her brings ome

nitary inspector called in to investigate a com of dampness, found an old house in a filthy state nily paid £1 a week in rent and their joint income 5 a week

es, in fact may grow up in overcrowded and ary homes and while they are at school their s are given statutory help in rearing them as one after another begins to earn and as some and bring home wives or husbands who are rning the family become affluent They will nsent to move into better quarters however, e they cannot be rehoused at the same rent they have got used to spending too small a proportion of their income on their accommodation One result is that others who have nowhere to live and little to pay, cannot even take over poor and cheap accommodation ' Not much more than a year ago ' Miss Poole reports ' a small local school had seventy of its children living with their mothers in night shelters ' Clearly it is absurd to subsidise rents for those who can afford to pay higher ones , and she suggests that housing authorities should use their powers more forcibly As those in condemned dwellings are evicted to make way for building so should the well-off families be moved from the slums, leaving for the time being the poor dwellings for the homeless or necessitous ' It is doubtful whether the housing authorities have the power to do exactly this but some way of getting round this difficulty should certainly be found in the interests of the children

The family of seven mentioned above have more than once refused to be rehoused on grounds of expense (they pay 12s a week rent) Most of the children have eye trouble because Miss Poole says while they were still at school the mother was not willing to lose time from work in order to take them to the clinic for treatment All are now earning and for the last two years the whole family have spent their holidays abroad (where admittedly they have relations)

With both parents at work children of school age spend a good deal of their time running about the streets but they are often expected to do the shopping and housework as well When they leave school and go to work even this amateur attempt at housekeeping goes by the board and despite a rising income the home becomes increasingly squalid But such financially prosperous families are not of course the only or most numerous residents of slums there are many people with young children living willy nilly under foul conditions Indeed conditions are inevitably foul where four or five families share a tap or a lavatory and use a common staircase which it is nobody s business to clean, where coal must be piled in the corner of a room, cupboards can be opened only if a bed is shifted and the slop pail and butter-dish are close neighbours Even more serious than such things as these is the effect on the physical mental emotional, and moral development of children of dishonest gross or terrifying neighbours

A family of six, known to Miss Poole, lived on the ground floor of a bombed house left in a state of disrepair On the floor above lived several men who boasted of thefts and illegal doings, used filthy language came in late at night, stamping shouting and singing bawdy songs and passed water on the floor above so that it dripped through the boards on to the terrified children in their bed

Life at close quarters with such ugly realities as drunkenness crime incest brothel keeping and the like damages the developing child in ways which we are only just beginning to recognise and assess As Miss Poole rightly comments rehousing is not enough human beings will have to be remade too She even doubts whether the modern policy of keeping the child in his own home—no matter how bad it is—is always fully justified A bad " dwelling may not matter much if it is illumined by the love of parents who do try to create a home however poor, for their children it is another matter, she suggests when the home is a filthy room into which the parents hardly ever come except to sleep The slum problem in fact, as the *Manchester Guardian*,[2] reporting the recent congress of the International Federation for Housing and Town Planning, pointed out, is still grave and pressing, and the question is how to make people in general aware of it

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[1] *Maternity and Child Welfare* 193[illegible] 16 13.

We are at this time, Professor BROCKINGTON notes, rather well placed for getting something done, since the rate of growth of our population is slowing down, and our numbers in this island are likely within a few decades to become stationary or to decline In a hundred years or so, perhaps the housing problem will have gone into reverse how to demolish reinforced concrete at small expense will then be exercising the planners In the meantime children are being stunted morally and emotionally, as they were once stunted physically, by the pressures of their environment The ideal of one family one dwelling, put forward by BROCKINGTON, is worth attaining quickly As things are, we are not only exposing our coming generation to harm we are laying on ourselves the onerous and costly task of remaking them as citizens

## Annotations

### OCCULT UNEMPLOYMENT

THE preregistration year, it is said, may take 15–18 months to complete[3] The time is lost mostly between the two house jobs, and, whereas formerly the newly qualified could put this "spare" time to good use by acting as locum tenents in general practice, now, without registration, any work outside hospital is barred to them.

This is a serious loss to the community Just over 2000 were provisionally registered in England and Scotland in 1954, and if 3 months is taken as the average excess over the working year required to obtain registration, then an equivalent of 1000 six month house jobs is being wasted annually If all 2000 could be more continuously employed the shortage of junior hospital staff would be felt much less acutely Considered in terms of highly skilled hands kept idle, the present position represents an unrewarding expense for the nation No business would permit the waste of such a valuable capital investment

How can the position be improved? The starting dates of jobs need to be related to the graduation days of universities and colleges Universities hold graduation days at different times, and, with many other faculties involved, they cannot be expected to fall into line with each other But most of the newly qualified take up appointments in their own teaching hospital or its surrounding region, so regional synchronisation would be fairly satisfactory Perhaps appointments to teaching hospitals should be made a short time before those to regional hospitals, in order to give unsuccessful applicants for teaching-hospital posts the opportunity of securing an appointment in the region without much loss of time Secondly, a proper appointments bureau is necessary—one central place in each region fully informed about the jobs that are to be had This is a function which many medical schools could fulfil more satisfactorily than they do at present

If in fact the average is lost about three months, regional boards might be asked to adjust the dates of appointments—though such is the inflexibility of the terms of the 1950 Act that an amending Act might be needed to enable the General Medical Council to register those whose six-month jobs were curtailed in the change over Nevertheless Governments will sometimes respond where man-power wastage is adding its toll to man-power shortage

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[2] Sept 21 1954
[3] See *Lancet* 1954, ii, 413

### COSMETIC PROBLEM OF ANOPHTH

REMOVAL of an eye sets a difficult cosmetic
which has not yet been satisfactorily solved.[1]
ately evisceration or enucleation is often l
junior staff After his socket has healed the
referred to an artificial-eye clinic, where a
supplies a concavo convex prosthetic shell wh
well and will be retained comfortably within
The resulting appearance is satisfactory only
with deep set eyes Critical patients rightly
that their new eye has neither the expression
appearance of the other eye, it occupies an
position and does not move

The normal eye rests on a sling of fascia
from the medial and lateral orbital walls This
ligament is formed by a thickening of Tenon's
the fascial envelope which surrounds the eye
of the extra ocular muscles and the lids pr
*dislocation of the eye, and the orbital fat forms*
behind it When the eye is removed the vol
orbital contents is greatly reduced, and the
ocular muscles adhere to each other and oblit
muscle cone The fat in the upper orbit thus
drop, and so the lower fornix accommodates
cushion of fat at the expense of the upper, whose
is greatly increased The usual prosthetic shell
ported in the shallowed lower fornix by the
orbicularis muscle of the lower lid, and in time
may become lax and everted because of the w
it bears The upper margin of the prosthesis rest
posterior limit of the enlarged upper fornix, so
to lean backwards, and the upper lid lacking the
of the normal eye may droop, with a sunken
above In the more fortunate cases the twitchin
fibrosed mass of extra ocular muscles at the
the orbit imparts some movement to the
cosmetically this is seldom adequate

The ophthalmologist's first difficulty is to
the eye with an implant which will keep the
fat and muscles in a nearly normal position
often been attempted, and many materials
introduced into Tenon's capsule glass, celluloid
peat moss, agar agar, rubber, wire, silk, catg
paraffin wax, and rabbit's eyes have all been
Smooth spheres of acrylic resin or of gold prov
reaction but tend to migrate Spaeth[2] reco
Guist's carbonised bone ball, because the
reaction which it causes firmly fixes it in its
location But, in truth, nothing seems really

Secondly, the ophthalmologist must provide
ment of the prosthesis by linking it somehow
implant Cutler[3] tackled this by inserting a
shaped acrylic implant with its opening facing
over which he closed Tenon's capsule, mus
conjunctiva These tissues were drawn at
into the basket by a button sutured to the
of the basket When healed the button was
and the conjunctiva remained dimpled The
had a peg which fitted into the dimple and thus
with movements of the implant But the
undergo pressure necrosis or may not form a
permanent concavity, and the long term results
much better than with spherical implants. Other
used *partially buried implants*[4 5] The co
covered the implant, leaving an exposed
which the prosthesis peg fitted accurately
ments of these prostheses were excellent, and
technique the lower fornix was relieved of the
of the prosthesis But Choyce[6] followed up 99

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1 See Dimitry T J *Arch Ophthal, Chicago* 1944 31
2 Spaeth F B Principles and Practice of Ophthal
London 1948
3 Cutler, N L *Arch. Ophthal Chicago* 1946 35,
4 Ruedmann, A D *Trans Amer ophthal Soc* 1945
5 Cutler N L *Arch Ophthal, Chicago* 1947 37, 73
6 Choyce D P *Brit J Ophthal* 1952, 36 123

uch implants and found that 45% were extruded three years because of infection He thought it ble that few such implants would be in situ five after insertion and for this reason he recommended tinuing their use

ing[7] has had an original idea for solving the tic problem He removes the contents of the eye ecures within the empty sclera an implant which ns a magnet the prosthesis also contains a et Young's implant maintains the structure of the in its normal state and the magnetic attraction plant to prosthesis imparts a full range of move Furthermore he relieves the lower fornix of n by the implant s magnetic support of the pro Young claims that his prosthesis which is thin not be removed more than once a month though es not state on how many cases he bases this usion If the long term results are satisfactory others can make his rather complicated method this technique will constitute a major advance

## ILDREN S HOSPITAL TO BE CONVERTED ?

RECOMMENDATION to the board of governors of ry s Hospital that the Princess Louise (Kensington) tal for Children should be converted for use by patients focuses attention once more on the ing pattern of supply and demand in the hospital es. The development of maternity and child e services, the advances in medical knowledge and ique and the improvement of economic and social ions are combining gradually to reduce the number spital beds needed for children and though this ituation must be a source of satisfaction and pride concerned it also raises the question of which beds to be retained and which can be used for other ees.

County of London has ten general children s als with a total of about 1000 beds and there are bly another 1500 beds in the children s wards of hospitals in the county This gives a ratio of 75 en s beds per 100 000 people and though one remember that London hospitals draw patients far beyond the county boundaries this provision atly in excess of the 50 per 100 000 suggested by o and Taylor in their estimate of the needs in astle[8] On this score it therefore seems probable a reduction can safely be made in the number of en s beds in London and the arguments put before Mary s board by its subcommittee are convincing far as they relate to diminution of need On the hand the subcommittee s proposals for dealing this situation by closing one of the children s tals are more debatable Some would say that it be better to preserve and develop the children s tals as centres of paediatric treatment and education o reduce instead, the number or size of children s in the adult hospitals serving the same catchment even if the hospitals concerned are not controlled o same boards or management committees The bility of doing this is not discussed in the sub ittee s report but it will no doubt be raised by the al s medical staff committee who are putting their ions to the plan before the governors

making their recommendations the members of bcommittee were properly influenced by the board s tion to provide facilities for clinical teaching and e relative pressure upon the hospitals under the s immediate control From this restricted point w the beds in the Princess Louise Hospital may be luous and so may those of several other of the on children s hospitals the majority of which are parts of teaching hospital groups Nevertheless se children s hospital have traditions and achievements of which they can be proud and before the drastic and controversial step is taken of converting any of them to other uses it would be prudent to develop more fully the arguments for and against the preservation of children s hospitals as such and to review as a whole the situation of children s beds in London. To make such a review is perhaps beyond the scope of any one of the 30 different boards and management committees that control the children s hospitals and children s departments of adult hospitals in London but it should be made before any final decision is reached

## TRANSFUSION OF BATTLE CASUALTIES

IN the latter part of the 1939–45 war blood loss was generally regarded as the most important cause of shock in battle casualties Usually the degree of shock was closely related to the volume of blood that had been lost but occasionally shock was more severe than might have been expected In some such cases the patients did not respond well even to generous transfusion and a few died The question of how many of these might have been saved by even more lavish transfusion has remained unanswered.

In Korea during 1952–53 belief in the importance of restoring and maintaining the blood volume after severe injury led to freer use of massive transfusions of blood Up to 30 pints of blood was given within twenty four hours of injury much of it after bleeding had been controlled Prentice et al[1] using the blue dye T 1824 or red cells labelled with $Cr^{51}$ studied the changes in blood volume after operation and massive transfusion in 53 severely injured men In 43 the initial body weight was known and their normal blood and plasma volumes could be calculated In only 3 cases did the blood volume rise above normal values—in 2 after 7 litres and in the 3rd after 1 5 litres, of blood Of 25 patients of known weight studied with $Cr^{51}$ 11 had blood volume deficits of less than 15% after transfusions averaging 3 187 litres in the other 14 the deficit averaged 32% after transfusions averaging 6 74 litres Despite these large deficiencies only 3 patients whose volume deficits were 38% 43% and 52% showed the clinical features of shock Of the 18 weighed patients whose blood volumes were measured with dye 14 had deficits of more than 15% the average deficit being 31% after transfusion averaging 7 785 litres; yet none showed clinical signs of shock, and all did well after operation

When the patients were grouped according to the sites of their wounds the importance of muscle injury became clear In wounds of the limbs there was almost always gross muscle injury and large volumes of blood were needed during resuscitation and operation Yet after operation nearly all these patients had a blood volume more than 15% below the calculated volume and their average hæmatocrit was 30 6% On the other hand patients with abdominal wounds who had received similar volumes of blood had postoperative blood volumes more nearly normal and an average hæmatocrit of 45 8% Prentice et al found that when large masses of muscle were injured large quantities of blood were normally required for resuscitation But it is remarkable that in a 78 kg man with a traumatic amputation a blood volume of 2 6 litres on admission rose only to 5 1 litres after an uneventful reamputation with minimal blood loss and the transfusion of 10 5 litres of blood In a similar case a transfusion of 3 litres raised the blood volume only from 2 5 litres to 3 0 litres It seems unlikely that much blood was lost into the tissues damaged at operation In abdominal wounds blood loss is chiefly due to damage to vessels in the intestinal wall and mesentery; and bleeding into the peritoneal cavity must be directly and accurately controlled by li at operation In wounds of masses of muscle in the limbs it is impossible to control all bleeding-points at operation, and the most that can be done is to ligate the obvious, larger vessels, after operation a good deal of blood is lost into the muscles in the margins of the excised wound, and there is always considerable postoperative swelling of the less severely damaged muscle in the region of the wound Whether this accounts for the lowering of the blood volume by a third found by Prentice et al is uncertain, but it seems the most likely of their three possible explanations for the discrepancy between blood volume and the large quantities of blood transfused They have shown that it is unlikely that blood is trapped in parts of the vascular system and is not measured by the methods they used, or that hæmolysis of the transfused or recipient's cells was so extensive as to account for the large deficits

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[7] Young J H Ibid 1954 38 93

[8] Spence J C Taylor M D Lancet 1954 i 719

[1] Prentice, T C., Olney J M Jun., Artz, C P., Howa Surg Gynec Obstet 1954 99 54

Of the 53 patients 3 received more than 10 pints of blood and 9 more than 20 pints, yet after transfusion the average deficiency in blood volume was 25% As the total volume of blood transfused increased so did the discrepancy between the volume administered and the subsequent blood volume, and this difference involved both red cells and plasma Blood volume did not rise later during recovery, as might be expected if blood had been sequestered during the acute changes after injury and operation Prentice et al suggest that further evidence may be obtained by weighing patients before and after resuscitation, in addition to measuring blood volume

At first sight this report suggests that most severely injured patients are inadequately transfused and that in future much larger volumes of blood should be given, but this impression may not be wholly correct After transfusion and operation most of the patients were in good condition despite reduced blood volumes, and as the amount of blood transfused increased so did the discrepancy between this and the final blood volume It is conceivable that much of such large transfusions may be lost into injured tissues and be metabolised there In severe infection and in peritonitis [2] blood volume may remain persistently depressed despite large transfusions of blood or plasma The cause is presumably disturbed vasomotor control, and a similar disturbance may follow severe injury

## SMOKE AND SULPHUR

We are all by now thoroughly convinced that smoke fog is a bad thing—destructive to life, health, and materials, light obstructing, dirt-begetting, and enormously expensive We owe warm thanks, therefore, to those who have demonstrated how much harm it does But it is perhaps a little disappointing that so much of the research in progress is still directed towards amassing more and more gloomy statistics about the effects of atmospheric pollution As Sir Ernest Smith said to the National Smoke Abatement Society last September,[3] "it should not be necessary to wait for absolute proof from statistics before tackling all the problems of atmospheric pollution in a comprehensive way"

As the Committee on Air Pollution (the Beaver Committee) [4] made clear, there are two main components in smog—namely, dirt and grit, and sulphur products The committee concluded that if this (or indeed any other) Government would declare for a clean air policy the dirt and grit could be abolished fairly quickly Thus it could be reduced by making much more smokeless fuel available for domestic grates, by popularising appliances for the economical burning of these fuels, by introducing modern plant, better methods o and a wider use of gas and electricity in indust better control of smoke from railways, by esta more smokeless zones and also smoke control a which the use of bituminous coal for domestic would be restricted), and by more effective (to be enforced by local authorities) against the of black smoke Such a programme might ve give us a sparkling—though not necessarily atmosphere in a very few years

But the sulphur products—the invisible more dangerous component of smoke—pres difficult problem The total quantity of sulphur discharged into our air is over 5 million tons a and at present we know of no really satisfactory preventing its discharge One straightforward pr measure would be the better cleaning of coal at t heads so as to remove as much sulphur as possi the National Coal Board is pressing on with a pr to achieve this, but only a small part of the be removed in this way by existing methods It possible to add some material to coal which woul the sulphur to be retained in the ashes, attempts this have not so far been successful, but further r might well give the answer Fuel oil, used in r and to drive some vehicles, also releases sulphur i air, but, though it is technically feasible to most of the sulphur from fuel oil, this is a costly p In large power stations sulphur dioxide can be from the gases, and such processes are used Battersea and Bankside stations, though not de The cost of installing new plant in other st Beaver Committee estimated, would add 8s to th of converting each ton of coal into power, or 0 unit of electricity generated—an addition which scarcely be dismissed as inconceivable At a discussion of the Beaver report, held by the Inst Fuel on Jan 21, this figure was challenged by M Peattie, deputy chief engineer of the British Ele Authority he thought the cost of intr washing into power stations would be at leas million and might be £250 million—which, h would increase the cost of electricity by 12% E expenditure, however, might well be justified committee's estimate of the damage done by air p in a single year was £250 million

His was the only critical note in a meeting pro Beaver Mr G E Foxwell, D SC, immediate president of the Institute, and a member of the Committee, suggested that our present difficult the fact that the National Coal Board and the gas are hesitating to expand smokeless fuel p because the Government have not accepted a policy, while the Government are hesitating to this policy because they are not sure whether, if the nationalised undertakings would be able to r additional demand for these fuels In an att break this deadlock, Mr Gerald Nabarro has int into Parliament his Private Member's Bill—the Air Bill This will come up for its second re Feb 4, and it embodies all except the fiscal mendations of the Beaver report It is a measure Dr Foxwell hinted, has been compared by so *spur to goad the Government to action*, and by o a pistol likely to go off at half-cock In Mr N own view, he said, the Government have no inte introducing legislation during this session a any measures to deal with air pollution would be till after next November, and probably fill t Parliament We should all like to see someth before that

One further reason for spending money on ne that the sulphur which is at present such a liabilit become an important asset Even the method ng used at Battersea and Bankside result in the rge of sulphur effluents into the Thames—an urable practice in itself and a shocking waste of modity which is always valuable and sometimes

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[2] Theron P H Wilson W C *Lancet* 1949, i 172

[3] The Coal Crises and Society Published by the National Smoke Abatement Society 30 Grosvenor Place S W 1 Pp 10

[4] London H M Stationery Office 1954 See also *Lancet* 1954,

At Fulham power station before the war a d was used which retained the sulphur as impure m sulphate but this method was given up during ar and has never been started again A new and er process, on trial by the British Electricity rity gives ammonium sulphate as a residue but ears are rolling by without any report appearing s method and the Beaver Committee remarked hey were not impressed by the speed with which matters have been pursued Perhaps some ive to speed might be offered

thing is abundantly clear we must agree as a s to spend more money on this problem To doctors sed to spend whatever is necessary seems urgent ven from the strictly economic standpoint there are arguments against the present conversion of so precious coal into useless smoke. Money spent on ering ways of preventing so much waste and ge may be expected to repay itself many times over

## CROWDS AND POLIOMYELITIS

a group of epidemiologists were asked to predict ffect of large crowds on a poliomyelitis epidemic replies might not be unanimous They and others herefore be interested in a careful account of what ned in a situation of this kind.[1] Western Australia, the most sparsely populated areas of the Common h experienced its biggest recorded poliomyelitis mic last year The only epidemic of comparable n this State had been in 1948 and on that occasion athering of crowds was thought to have had an se effect on notification-rates

t year's *epidemic* coincided with the arrival in rn Australia of the Queen and the Duke of Edin , and huge crowds were expected throughout the The public-health authorities felt justifiable alarm he possibility that the crowds would allow the mic to spread and enlarge Precautionary measures attempt to reduce the spread of infection in crowds, aimed largely at children A special review of ren which would have involved mixing of children many different areas, was cancelled Instead en were assembled in their own school groups at l points on the highway of the Royal route ren were not required to stand about for longer an hour and each child was given a health bag ining food a drink, a cake of soap a small towel his or her own drinking vessel School groups kept carefully apart from each other but no l measures were taken to control the size of adult s General control measures were already in opera Clinical cases of poliomyelitis were isolated for weeks and close contacts under the age of 15 were at home for the same period There was a publicity aign on the importance of hand cleanliness, and ier on anti fly measures *Dental operations* tions on the nose and throat and immunising ions were suspended and swimming classes were lled

e Royal couple arrived in Western Australia just the peak of the epidemic, and crowds of sizes ecedented in the history of the State gathered every f the following week These crowds were extremely s and yet the steep downward trend of the notifica rate was quite unaffected This can hardly have due to exhaustion of susceptible individuals for onths after the epidemic peak there were still over tified cases a month—a figure regarded as within the mic level for Western Australia

We are left with the possibility that crowds are not an important factor in the spread of poliomyelitis or that the precautions prevented increased spread Nature is an untidy experimentalist, and because of the absence of controls in most of her trials it is almost impossible to assess the importance of different factors Nevertheless either conclusion would point to transmission of infection by fæcal contamination as more important in this epidemic than spread by pharyngeal droplets This is in line with the seasonal incidence of the disease and with the higher concentration and longer sojourn of the virus in the intestine than in the pharynx The experience of the Western Australians has valuable lessons for epidemiologists everywhere

## NATIONAL FORMULARY

THE 1955 edition of the *National Formulary* will be welcomed by both general practitioners and pharmacists for whom it is principally designed This volume retains the general structure of its predecessors and an admirable dogmatic survey of current pharmacological teaching will be found as before, in its opening pages The formulæ themselves represent a wide range of prescribing traditions The Joint Formulary Committee announces that its policy has been to retain a prescription even if its justification on pharmacological grounds is disputed provided it is still in common use This spirit of leadership from behind explains the retention of many favourite prescriptions but not the *rejection of the* pill of aloes the emulsion of liquid paraffin with agar or the compound thymol mouthwash But room has to be found for many new preparations and something must go one can imagine that each of the 62 deletions cost the committee a pang The capsule of quinalbarbitone and the tablet of isoniazid are welcome newcomers but it is strange to find among these mist. gent alk c phenobarb and tab quinin bisulph

In the 1952 *Formulary* each preparation had a Latin and English title in that order whereas the section headings had an English and a Latin title in that order Consequently the pulveres were sandwiched between cataplasma and the liquores This arrangement, according to the new preface proved inconvenient to the users *of the Formulary But now instead of adopting the* obvious solution (as in the *B.P* and *B.P C*) of finally displacing all Latin titles to a position of inferiority, and calling all things by their plain proper English names the committee has turned the clock backwards Poultices are now followed by collodions and these in turn by nasal washes The main titles of preparations are given in abbreviated Latin displeasing to the eyes of those who read Latin and meaningless to those who do not The *Formulary* contains a pharmacological classification but in its present form compressed into 15 consecutive pages, this is little more than an additional index The classification would be much more valuable if its sections were dispersed throughout the *Formulary* proper which would then be a suitable companion volume to the modern textbook of clinical pharmacology

Meanwhile these criticisms should not obscure the general excellence of the book which is a sturdy monument to the British tradition of compromise If publication of it were to cease its sternest critics would be among the first to protest The *Formulary* is to be distributed to doctors next month Distribution also to clinical students might greatly encourage rational prescribing with a *corresponding decrease in the national drug* bill

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Dr C. H Hampshire, secretary to the British Pharmacopœia Commission from 1929 to 1950 died in London on Jan 23 at the age of 69

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[1] Snow D J R *Med J Aust* 1955 1 2.

[1] National Formulary 1955 London British Medical Association and Pharmaceutical Press 1955 Pp. 410 5s

## Public Health

# HOUSING

## FROM THE FIRST WORLD WAR TO THE PRESENT DAY *

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THE story of housing is one of the most dramatic and poignant in our social history Two of our most cherished beliefs—the ideals of health and of property—have been brought into conflict over the issue of the sort of home in which we should live It has been a struggle waged, as it were, between giants, and fought on shifting sands As property rights slowly conceded point by point the right to State intervention, the demands made on the score of health increased in step, as the measures to combat slums gained in cogency, the increase in population and the rise in households continually tended to neutralise their success In the background of the contest lay the bogy of overcrowding, worse perhaps than the slum itself, which was made greater by slum clearance

Looking back at the seventy years preceding the first world war, one may ask why so much legislation over so long a time had so little effect The trouble lay mainly in the failure to meet four fundamental difficulties (1) the inflated cost of building land, (2) the need to compensate owners of demolished slum property, (3) high rents of new houses, and (4) the difficulties of slum-clearance in circumstances where populations and households were ever expanding When great overcrowding and widespread slum conditions are present together, the administrator who presses for the demolition of the slum, unless he also provides the equivalent in new housing, ipso facto, increases the overcrowding From the frying-pan into the fire, some would say Nor was the obvious truism always appreciated that in the slums live the poor The costs of new housing are so high that rents, if unsubsidised, are beyond the pocket of the slum dwellers Legislation that takes no account of these fundamentals must always be a dead letter Such increases in new housing as there were took place chiefly by trends and influences independent of Parliament Such houses were not for the unskilled and semi skilled workers, whose lot remained largely unaltered In any event, the increase in the number of households was sufficient to occupy all the new dwellings built under private enterprise

To all this was added the difficulties of advancing standards The number of dwellings needed rises as the number who can be supposed to live properly in a home goes down The difficulty of providing them becomes greater as the standards advance

### The Inter-war Period

The first world war left the state of housing graver than before By 1921 we had reached 8,739,197 households, and $3^1/_2$ million persons were living, in England and Wales, at more than 2 per room In Scotland the figure for overcrowding was 43 3%, with 21% at more than 3 per room. But as we enter the period between the wars we find increasing evidence of a new outlook The Housing Act, 1919, required local authorities to prepare schemes for providing in their areas enough homes for the working classes and at first the Government gave unlimited aid, by paying excess cost over a 1*d* rate But the enemy of increasing cost soon gained the upper hand the 1923 Act limited Government aid to
tribution of £6 per house per year for twenty
that of 1924 (the Housing Financial Provi
to a subsidy, with restriction on sale, of £9 for
years in urban areas and £12 10*s* in agricultural
Between 1918 and 1931 over 1 million houses were
three quarters of them under government
schemes, and between the wars the grand total
4 million homes The volume of house buildi
1930 rose to an average of over a third of a
a year

The Housing Act of 1925 left much to be desir
it stimulated the first real efforts at slum-cl
and those of 1930, 1935, and 1936 made a valiant
to deal with the remaining difficulties The
removed the liability to compensate owners of
houses when these were made the subject of a de
order It required houses to be provided in
for clearance areas, thus removing another great
to action, and it introduced a new procedure
"improvement area"

In 1935 overcrowding was at last officially
This was on a low rating roughly similar to the
room scale used by the Registrar General for
forty to fifty years in his Decennial Census Auth
were required to survey their areas and report
extent of official overcrowding

The 1936 Act brought the legislation to its
state The responsibility rests with the housing
ties, as it has done since the beginning, to insp
districts, the authorities have the power,
appeal to a county court, to order unfit houses th
be made fit at reasonable expense, to be repaired
ing to a schedule of work Houses that cannot b
fit at reasonable expense may be the subject of a
for demolition or closure, Any areas consistin
least two houses may be declared a clearance
a clearance order can be submitted to the Min
Health for confirmation, there is provision for re
ment areas, which has extended the idea of the
ment area to include all property in a given are
there is authority for compulsory purchase orders,
with the power for making by laws. Al
applies to houses that are occupied, or are of th
suitable for occupation by persons of the
classes

It was unfortunate that the Housing Act
allowed a variable standard of fitness to continue,
that of the "general standard of housing accomm
for the working classes of the area"

The rate of clearance accelerated By 1939
of a million houses had been demolished and
had all been made good by replacement hous
much of the benefit of the vast slum clearance
through the overcrowding which remained W
second world war this intense activity came to
and all further attempts to destroy slum propert
left to the enemy

### After the Second World War

The post-war period has been one of intense
activity, unassociated this time with any atte
remove the slums, and accompanied by a new
to town and country planning Since the war
2 million houses have been built, five eighths of
local authorities, and 124,555 in temporary
There can be little doubt that almost for the fir
have gained a lead in overcoming overcrowding Th
however, is not great, for the influences that
the need for separate dwellings have been exc
Within the past quarter of a century—betwee
when there were 10,154,000 families, and 1954, wh
were 12,152,000—there has been an increase of

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* Part of a lecture contributed to a series on the Changing Social Environment 1850–1950, delivered at the Uni Cambridge on Oct 25, 1954

1 This was the figure on June 23, 1954

ing separate accommodation. This includes the red and single adults who nowadays more often to live alone.

idea of planning the use of land was first intro in 1909. The 1919 Act required all boroughs and districts with over 20 000 people to produce a e of development. Again and again Parliament l measures (in 1923 1925 1929 1932 and 1935) ied to strengthen the control of land but with real effect. Only 5% of England was by this means subject to a planning scheme. With the second war however real appreciation of what was d for control began to grow up. In 1943 a separate ry of Town and Country Planning was created— ng the Government's acceptance of the belief that planned use of land was ever to become a reality ld only be as a result of action on a national scale Barlow, Scott Uthwatt Reith and Hobhouse formed the basis of a new machinery. The Towns Act 1946 was followed by the Town and ry Planning Act 1947. Twelve new towns have been d and the planning authorities—now limited to the councils and county borough councils 145 in or—have been preparing schemes for their areas.

### The Present Position

lay we hear more complaints than ever but they out of an awareness of what good living demands of se. It is only in the past fifty years that internal ing sanitary convenience and bathrooms have to be considered a general need. The Housing f 1923 was the first to require a bath in a new ng and that of 1924 a bathroom. Our present ards owe much to the work of the Central Housing ory Committee appointed under section 135 of lousing Act of 1936 and to the *Housing Manuals* 44 and 1949 which this committee produced. To 44 manual we owe the 16 point recipe for the making healthy house. The Housing Act of 1949 has seen nd of varying standards of fitness according to tate of the working class property in the area. as extended the jurisdiction of the housing authority lly to all property. We have also come at last to ciate that overcrowding is more damaging to comfort, and enjoyment than is the insanitary of the dwelling itself.

housing today falls far short of the ideal.

*owding*

rcrowding is still a serious consideration. Accord the 1951 census 11.6% live at a density of between $1^1/_2$ per room 4.9% between $1^1/_2$ and 2 per room between 2 and 3 per room and 0.4% over 3 per (For the purposes of the census rooms counted he usual living rooms including bedrooms and n but excluding sculleries landings lobbies closets bathrooms.) Improvement in official overcrowding between the 1931 and 1951 censuses had been ectedly high. The average of persons per room has from 0.83 to 0.73 in England and Wales and from o 1.01 in Scotland. The percentage living at more 2 per room has fallen from 6.91 in 1931 to 2.16 51. In the 1931 census there was only one London gh with less than 5% of the households living at per room. There are many areas (e.g., in and around astle and Glasgow) where overcrowding is still a. The average density per room in Glasgow is and a recent survey of 718 families rehoused for years showed an average density of 2.03 per

t overcrowding is more serious than these figures at. The official figure for overcrowding which is roughly 2 per room is too lenient. The figure of the Royal Commission on Population is 1 per room. At this rate there were just under 3 million households holding over $13^1/_2$ million people, overcrowded in 1951. Further to this overcrowding affects the family and particularly the large family. Overcrowding increases steadily with family size. 44% of families with 5 persons has less than one room per person; the figure for 6 in a family is 72% and for 8 in the family 93% according to a special survey quoted in the report of the Royal Commission on Population. This rise of overcrowding rate with family size takes place equally within the same income group. We have also to remember that many more households although not technically overcrowded, live an overcrowded life. The chief cause of this is lack of warmth which may cause 3 or more to crowd into a bed or 5 more more to a small room.

The effect of overcrowding in the absence of other adverse factors are in 1954 not easy to assess. Housing is one of a number of factors which play their part in the spread of infections of the respiratory type. When other important adverse influences are absent, overcrowding on its own may be relatively unimportant as the cause of illness. But when other things are not equal over crowding in an unhygienic house may be the determining factor. It is thus with tuberculosis once an open case occurs in a house secondary infection of children becomes more common. It is thus also with infant mortality and infections of childhood. But much the most important effect of overcrowding is its destructive influence on an ordered family life. No true home life can be lived in an overcrowded house.

*House sharing*

Overcrowding is objectionable and can lead to physical mental and moral ill health. Sharing of dwellings is no less an evil. It is itself a cause of overcrowding and a potent source of mental strain. Over 2 million house holds in Great Britain (1951 1% census) are shared, $^1/_2$ million of these are also overcrowded (that is living at more than 1 per room). Sharing bears heavily upon those with young growing families and particularly upon the newly wed. In a recent Aberdeen study of women who booked a bed for a hospital delivery over half of the total and about three-quarters of the primigravidæ shared a home. The most inadequate and often insanitary accommodation can be preferable to sharing. Insecurity worry and unhappiness are the results of the conflicts which arise.

*The Poor Home*

The outlay required to get a roof over your head varies with the choice and area and structure. Good housing in a healthy area will generally cost more than a slum dwelling to rent. The significance to the family budget of this simple fact is considerable. Children cause poverty and poverty is the chief reason for the poor dwelling. Large families suffer particularly. As the family grows and the weekly pay packet has to be stretched to meet increasing liabilities the parents before sacrificing food seek relief in cheap clothing and less expensive housing. The large family naturally gravitates to the cheapest sort of house. An alternative is to increase the family income by taking in lodgers or sharing. The growth of the family is probably one of the reasons why in the Aberdeen survey council houses occupied by such families were more commonly shared (78% as compared with 38% of private dwellings). Council houses were also more often overcrowded (29% as compared with 14%). Indeed any influence that takes away the element of elasticity in the budget may do harm. In the M'Gonigle survey at Stockton-on-Tees the suggestion first appeared that re-housing could be harmful to health if the cost of housing was too great for the budget. The flexibility of cheaper housing was

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erguson T Pettigrew M G *Glasg med J* 1954 35 153 removed Soutar, Wilkins, and Sargant Florence[3] said of the Birmingham survey

> “While providing a much better environment the housing estate undermines the family's resources in other respects The family moving from the slums to a new housing estate on the edge of the city has greater costs to meet out of the same income Rent is usually higher, there are increased costs of transport both for business and pleasure, and often the necessities of illness, there is usually a need for more furniture, necessitating hire purchase agreements, wear and tear on clothing, especially on footwear, is generally greater, children's appetites are increased, food prices are higher *To accentuate these higher costs there is sometimes* a reduction of income due to women losing the opportunity for part-time work in the city As an independent social reform, rehousing has its limitations”

### *Lack of Equipment*

Despite the big housing drive, many of our present houses are obsolete Out of our total of about 11 million houses, nearly half were built before 1914 and 3 million before 1870 In the matter of housing we are living in the past The 1951 census recorded more than 1 in 5 households (22 7%) without exclusive use of a water closet and twice this number (45%) without exclusive use of a fixed bath More than 1 in 10 (13 8%) are without exclusive use of both sink and stove For the 57,700 households with more than 3 persons living per room the present situation is grossly inadequate, 52% of these are without exclusive use of a piped water-supply, 41% lack exclusive use of a cooking stove, 80% of a kitchen sink, 84% of a water-closet, and 92% of a fixed bath 84% of these overcrowded homes lack exclusive use of both stove and sink There are 2 million households (2,078,800) sharing dwellings, irrespective of the number of rooms occupied, that present a similar picture, the percentages of inadequacy (64, 39, 49, 69, 86, 50) being very similar to the houses living at 3 per room In half of these shared dwellings, where the household lives in one or two rooms, the percentages of inadequacy (78, 57, 69, 86, 94, 70) are almost terrifying in their completeness The term “living” in such conditions is an exaggeration Even to consider the usual inadequacies of bedroom space, furnishing, the absence of a pantry, a broom-cupboard, or proper space, heating, and lighting, with room for children to study, and the many other essentials of decent living, seems fantastic in the light of such conditions

### *The House in its Social Setting*

Many of the social needs of the family should be satisfied within an area that can be conveniently reached The satisfaction of many of these will be found in the town The town, therefore, should be a pleasant place in which to live and a joy to visit it should shelter the good life That it ceased to be so during the hundred years between 1750 and 1850 is one of the heavy prices we have had to pay for industrialisation “The idea of the town,” the Hammonds said, “as a focus for civilisation, a centre where the emancipating and enlightening influences of the time can act rapidly and with effect, the school of social arts, the nursery of social enterprise, the witness to beauty and order and freedom that men can bring into their lives, had vanished from all minds” The town was no longer “a living personality, expressing and cherishing the instincts, tastes, beliefs and corporate pride of the citizens widely and richly pictured”[4]

## The Way Ahead

Bad as in many respects housing is today, our towns are immeasurably better than the civilian barracks and camps of 1850 Nevertheless, when one thinks of other achievements of our vast industrial mach balance sheet of a hundred years of housing encouraging

Perhaps the greatest hope of improvement li static population Britain, having battled its w two centuries along a dynamic demographic is now entering upon a period of stationary lation For some time to come—possibly fo years—this island will return each year to the Re Generals' departments a population figure of 50 million During the last twenty years or *independently of rising population*, the numb separate households has much increased, beca smaller families and the greater numbers of persons living alone This source of increase, likely to disappear With the old enemy halted we can overcome him completely The present d for new housing, if continued, should be overcome the present shortage, of which shared d is the most obvious sign, in a relatively short of time, and it can then be applied to the of the slum itself There is of course much to but in a static population and without the tion of increasing households the task is well our capacity We will be wise to remember the of Lord Simon of Wythenshawe in the 1930s worst living conditions are not to be found in slu in the overcrowded larger houses let in lodgings shall also be wise to continue to let new buildin priority over slum-clearance

Nevertheless, the time has come to look b immediate needs Quantity has necessarily taken of place in our thoughts we have needed so the roof over our head But now that the ideal family, one dwelling, is at least within our gra should turn our attention, without delay, to quality should seek to provide for the good life by enri interior of the home and by adorning its social se

### *The Home*

It is not for me to talk about architectural detail I will only speak of the home itself As Mack says, “In dealing with ordinary families, planning too often been a dull, routine matter of figures, to family size, and houses and flats are acc built with one, two, three, or more bedrooms in to certain mechanical calculations”[5] To think in of persons per room, as now we are inclined to often to ignore the meaning of family life Our aim be to provide what is needful for a home, including diverse objects as hobbies for father, and a roo study and quiet for grammar school children We aim at good insulation and proper space heating can now make it possible to use every room for older folk and single workers, every home have three bedrooms A newly married couple, *family to start and to carry through*, and later children's friends to put up, can look forward occupation of a three bedroom house for a cont spell of thirty years The home must cease to woman's workhouse Good planning and the technical aids, which the New World has sp can release her from drudgery The framework of services from space heating to clothes washers, be mass produced, freed from the exp inadequacies associated with lack of uniformity made available to all at home The house must be than a reluctant and passive partner in family E should be an active, willing, and friendly particip

### *The Town*

One of the most important needs of a good social is that there shall be an easy access to a cultural eed good towns If this was true in the 17th century much greater the need today when we have become ion of town dwellers Good towns were relatively o produce when this country had a population of e 8 million people and a strong rural economy he proper balance of town and country is im ly *more difficult with 50 million and a strong* industrial economy Yet it is not impossible l is the great enemy and must now be strongly ed

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[3] Nutrition and Size of Family Report on a New Housing Estate, 1939 Prepared for the Birmingham Social Survey Committee by M S Soutar E H Wilkins and P Sargent Florence London 1942

[4] J L, Hammond B, The Town Labourer (1760– don 1949

[5] Mackintosh, J M. Housing and Family Life London

goal we should place before us is to recreate our . For this some measure of compactness is needed elopment and in filling should take preference further extension of our urban areas

hile the creation of a new community is often th st and most attractive task for the skilled technicia *Housing Manual* 1949 says, the need for lou z all s possible to remedy the deficiencies of existing lev lop should not be overlooked ; this work is less spectacular effect upon the general wellbeing of the community whole as well as the occupants of the new houses are built, may be even more important and far ng

r towns have suffered two centuries of agony It o now to treat their wounds In advising local rities on what principles they should plan the *ing Manual* of 1949 says very wisely In most towns there are substantial areas surrounding or diately adjoining the business or central area that n need of redevelopment It advocates that ividual re-development schemes must be related o redevelopment of a town as a whole and care be taken that all first stage redevelopment is ly related to a complete and comprehensive e" This should offer the opportunity for restor he proper balance of open space and for providing nably accessible playgrounds parks and gardens must not be afraid to go upwards when this is part ell ordered plan

good town will have scope for a wide variety of and heights of buildings. We have given favour e cottage but in point of fact there are many tages structurally and æsthetically in the terrace detached two storey cottage of standard design ckintosh has said is usually an unpleasant looking box *inclined to be cold in winter* The terrace is and without making serious inroads on privacy lts of greater variety in layout of the estate as a , and in the treatment of separate blocks How of 17th-century English beauty of architecture e to the terrace

r the *improvement of our social setting* our greatest must now lie in the Town and Country Planning of 1947 The Industrial Revolution, achieved at a of reckless misuse of land has left us a legacy of *rn towns sprawling suburbs and disfigured* ryside Time will be needed in its remedy To e should now bend all our efforts

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The curse of religions is their tendency to make people e that certain systems of doctrine and certain cere s contain in themselves the whole secret of the universe educing the vast and wonderful to the small and childish tunately when human nature functions without religion kes exactly *the same mistake* The blight of modern ology is its tendency to think that when names are to various aspects of human behaviour a great advance ds wiser conduct is thereby made Similarly the nce of priesthood is to-day found all too frequently g scientists and notably psychiatrists. The nature of iverse and of man is in hard fact infinitely complex and ntely mysterious it makes ridiculous those who d to know all the answers whether they do so in the of God or of science —*Observer* editorial Jan 16

## HEALTH EDUCATION

The education of the public in matters of health is no new practice but whereas formerly it was haphazard and desultory it has now become methodical and systematic Yet even in this country there is evidence that it should be intensified

David[1] showed that in Greater London people were surprisingly ignorant about tuberculosis—although there has been more propaganda about this disease than any other Half those questioned thought that tuberculosis was hereditary and a third either believed it to be non infectious or did not know whether it was or was not Gore and Hartston[2] recorded very similar findings Likewise a survey among women has revealed prejudice and ignorance about the causes and the treatment of cancer[3] Public ignorance—and apathy—are suggested by the tardy response to clean food campaigns the high home accident rate the continued vast expenditure on 'patent' medicines and the low rate of immunisation against diphtheria (It is estimated that *in the London area in 1953 only 51% of children* under 5 years of age had been immunised against diphtheria at any time[4] whereas the aim is immunisation of 75% before the age of 1 year)

Walker[5] speaks of the prevalent ignorance about medical science but does not doubt that today people are *more responsive to propaganda than formerly Partly this* improved responsiveness may be due to the experience of the many who were in the Services in the late war when a vigorous health-education campaign contributed *substantially to the ultimate success* of our arms Much of the most telling propaganda had its birth in the units themselves where it was fostered by the commanding officer and his officers with the medical officer as counsellor Some may recall too the posters and road signs on the highways of North Africa and Southern Europe Blood toil sweat and tears: why add Malaria? Mepacrine a milestone to victory' and others less polite. The obvious loss of man power through malaria dysentery typhus and other diseases was one of the most effective of all health propaganda weapons And contrariwise, in civilian life today one reason why rates of immunisation against diphtheria and smallpox are dangerously low is that so few parents of young children are old enough to remember the time *(not so long ago) when diphtheria was a serious menace* while still fewer know from experience what smallpox can mean But some of the Army's other educational weapons could certainly be more widely adapted to civilian conditions—for instance, with the managing director cast as the commanding officer and the works doctor as his counsellor

A W H O expert committee which has been examining this problem[6] recognises that health-education programmes can conform to no standard pattern the programme must be specifically designed for the locality As to methods the committee rightly criticises the long lecture which seldom secures continuous attention, and whose *effects fade rapidly* The lecture is slowly being ousted by the discussion group and panel discussion Films too have an important place but the committee points out that these may produce a passive mental state and in any case they should portray local conditions. Pamphlets and posters are increasingly used but they are quite costly and the committee sensibly suggests that if used at all they should not be put up simply as decorations and should be changed often. Similarly, health exhibitions may not justify the financial outlay unless they are followed at once by further local propaganda.

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[1] David, S T *Tubercl* 19[illegible] 33 78
[2] Gore A T, Hartston W *Mon Bull Minist Hlth Lab Serv* 1953 12 131
[3] Paterson R, Aitken-Swan J *Lancet* 1954 ii, 85
[4] Report of London County Medical Officer of Health 1953 See *Lancet* Jan. 8 1955 p 93.
[5] Walker J A *Med Offr* 1954 92 331
[6] Expert Committee on Health Education of the Public First Report *Tech. Rep. Wld Hlth Org* 1954 no 89

The report makes it clear that the aim of health education should be to encourage personal responsibility. In this country the Services continue to play an important part by training National Servicemen in hygiene and health. But we should now be concentrating on younger people, in pre school and school days.

### Vital Statistics for 1954

The Registrar-General's provisional vital statistics for England and Wales for 1954[1] show that the birth-rate was 15 2 per 1000 population, compared with 15 5 in 1953 and 15 3 in 1952. The infant-mortality rate was 25 5 per 1000 related live births, the lowest annual rate ever recorded in this country; this rate compares with 26 8 in 1953, 27 6 in 1952, 29 7 in 1951, and 52 8 in 1938. The death-rate was 11 3 per 1000 population, compared with 11 4 in 1953 and 11 3 in 1952. R births exceeded registered deaths by 171,334

### Influenza

In the 160 great towns of England and Wal were 134 deaths attributed to influenza in th ended Jan. 15. In the three preceding week had increased steadily, the figures being 56, 82, Since the week ended Oct. 2 there have been 64 from influenza in the 160 great towns; the corres figures for the three previous winters were 200 (1 426 (1952–53), and 261 (1953–54). Laboratory in tions continue to confirm that many outbreaks to influenza B, though isolated cases of influ have been identified in Wales and the Midlands

### Smallpox in France

A message dated Jan. 14 from the French mi public health and population gives the number of smallpox in the Vannes area as 44, of whom died (later press reports put the number of dea Contacts have been placed under strict surveilla mass vaccination has been carried out in the The latest cases appear to have been direct previous cases

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[1] Registrar General's Weekly Return no. 2, 1955. H.M. Stationery Office. Pp. 20. 1s.

## The Widdicombe File

### XXII ὁ βίος βραχύς

MY DEAR BILL,

Mrs Wayneflete has just died. Admittedly 83 is a good age and everyone will say she had a good innings, but I still feel sad. What a pity she didn't call you earlier instead of letting her daughter, who, as a one time nurse, surely should have known better, go on applying hot fomentations to an obvious epithelioma of the vulva. When my house surgeon finally got the history, we found that the original small swelling was first noticed *fifteen months ago*, and although it was at first thought to be simply a boil—and it obviously became infected very early—the fact that it grew bigger and bigger should have convinced her daughter that it was a most unusual boil! I believe the old lady herself resisted the suggestion that anyone should examine her, so the daughter, I suppose, is not wholly to blame, but they both became alarmed by the first hæmorrhage. You saw the specimen—I keep a coloured slide especially to show the students as a "horrible example."

As you know, I did a very wide excision of which even Stanley Way would have approved, but she had a local and pelvic recurrence rather less than a year later and from that moment went down hill very quickly indeed. Still, she did have about a year of reasonable comfort and I am quite sure the operation was justified.

I saw a very similar case in which the mother in-law of a surgeon had a melanotic sarcoma of the labium major which she had *known* about for eight months before seeking advice. Only a local excision to relieve the bleeding was possible, but in spite of the limited surgery she survived, spent a very happy six months in Devon—"down tu Budleigh Salterton"—and then mercifully succumbed with dramatic suddenness to secondaries in the lungs.

I expect you see tragedies just like this in your own practice—I only see the gynæcological ones, which are bad enough—and it does seem, on the face of it, that the public do need some education and reassurance about cancer.

And yet it is astonishing how hard it is to convince people—men, women, doctors, public authorities, even Government departments—of the necessity for *some kind* of health education. Stocks, in his "Studies in Medicine and Population Subjects" of 1950 produced some very alarming statistics. In the first place, of the 86,000 people of both sexes who die each year of cancer, 2 in 3 50 years of age and 1 in 5 is under 45—it's by no means a disease of the aged—and of these, ca of the breast accounts for about 1 in 5 and of the and adnexa for about 1 in 10. The tragedy women is that Stocks found that the avera between the onset of symptoms and the comm of treatment was six months for breast and t ten months for body of the uterus, which is enough reading.

Malcolm Donaldson analysed these statist further and showed that for carcinoma m "delay period" of *under* six months meant that 3 cases were stage I or II, and therefore more ame treatment, and in any case gave over 40% five ye rate.

In our own unit, we see about 50 cases of carc the cervix every year. Of these, 6% are stage I a are stage II. In not one of five major centres in F was the percentage of stage I carcinoma of the less than 11. The figures from the eighth annua on the Results of Radiotherapy in Carcinoma uterine Cervix (Stockholm 1954) show that, of cases analysed, 19% were stage I and 40% The five year cure-rate of 26,555 cases treated latest five years was 62% for stage I and 43% for and it was only 8 5% for cases in stage IV, who rep 1 in 13 of all cases seen. In 1955 it is still true to of all the cases of carcinoma of the cervix we se 1 in 3 will survive for five years. In our own se 1 in 4 at best.

It is quite obvious from this evidence that the the women come for treatment the better are our of helping them; so the delay must somehow be The Central Council for Health Education has t objectives: (1) to reduce this delay between fir toms and attending a doctor, and (2) to reduce th between reporting the symptoms to a doctor an effective treatment. Which seems reasonable Both the women and the doctors need ginger believe, for in my own experience not every menopausal bleeding" is sent to hospital by the at once.

Why should there be these delays? Some the mental state of the woman prevents her seek advice. Either she is ignorant of the significance symptoms, or she is so afraid of cancer that she to be told it *is* cancer in her own case. I alwa the students that all women are liars and all wo fools, which gets me into much trouble, altho force of the argument is never more fully shown these very cases of cancer in women. It does se women must be educated somehow to recog dangers they run in neglecting early and p

cant symptoms—the question is how I know
agree that wholesale propaganda would be worse
less and only increase the dread of cancer that
oman has but it is equally futile I think to say
y attempts at education would *introduce* fear of
I believe the dread is there already You read
valuable report, full of interest and significance
rson and Aitken-Swan in *The Lancet* of Oct 23
ic Opinion on Cancer They wanted to find out
y women put off seeking advice for symptoms
*spect* to be due to cancer The paper can t be
ised, it must be read in full but it did show the
g ignorance among women as to the nature and
of treatment and the obvious need for education
ust quote in full two significant passages

> er of the cervix is predominantly a disease of th
> ual groups yet it is in this class that ignorance of th
> is is most profound
>
> great majority of women realise the possible signifi
> a painless lump in the breast but there is no sense of
> *when cancer is so widely believed to be incurable*

lics are mine. Half of the patients with what
spected as cancer of the breast delayed seeking
or three months or more and 1 in 5 for *over a year*

can be no doubt that your way of discussing
blem with your patients is the best but (let us
ally frank) not every general practitioner is as
itious Not long ago a case was quoted in the
press of a man of 46 who went to his doctor in
er complaining of a lump in the throat followed
hagia In spite of deterioration and persistence
toms he was not referred to hospital until *seven*
later when a gland in the neck appeared By
had a hopelessly inoperable carcinoma of the
and in quoting the case the writer asked
we couldn't manage better education of the
and *of ourselves*

time ago the British Empire Cancer Campaign
t 21 040 *letters to general practitioners* asking
whether they thought education of the public
cancer would be of value 4831 replies were
l (about 24%) and of these 2148 gave an
fied Yes,' and 2683 an unqualified No
these *figures it was deduced that general practi*
were *not* in favour of cancer propaganda But
quite rightly pointed out that such a deduction
y misleading and in fact a misuse of statistics
fact, more than three quarters of the doctors didn t
the letter at all and only one doctor in *eight*
said 'No Lord Horder in reporting the
of the inquiry said that the Campaign expresses
itude to the General Practitioners in the country
ying in such large numbers This is an index of
erest which the problem arouses I never quite
ood why a 24% reply was considered a tremendous
s, while the fact that three quarters of the doctors
reply at all seemed to me to be an index of their
*nterest* in this vitally important matter

you there is a lot of opposition to the suggestion
medical officer of health should preside over any
tee to implement the scheme contained in the
y of Health circular (18/53) encouraging local
ties and voluntary bodies to initiate exploratory
s in cancer education For this and other reasons
failed completely to get a scheme started but
York and Manchester pilot schemes giving such
gement we must try again I am completely
ed it s worth it particularly when I remember
ayneflete

Yours ever
PETER GURNEY

# In England Now

*A Running Commentary by Peripatetic Correspondents*

NOWADAYS when public-school fees are so high and when about a third of the local rate is spent on education it is interesting to recall how some parents arranged for their children s education two hundred years ago

A gardener who became a nurseryman and later a small farmer sent his son, then about six, to a small school about a mile distant and later found a young teacher to teach this elder and his younger son nearer home With him they learnt to read English tolerably well and to write a little Gilbert, the younger was too young to profit as much as the elder Robert who soon became remarkable for his fluency and correctness of expression and read the few books that came in his way with much pleasure and improvement Their education continued thus three years when the little seminary was broken up by reason of the master obtaining a superior situation elsewhere

The farmer then instructed his sons himself He conversed familiarly on all subjects with us as if we had been men and was at great pains as we accompanied him in the labours of the farm to lead the conversation to such subjects as might tend to increase our knowledge or confirm us in virtuous habits He borrowed Salmon s *Geographical Grammar* for us, and endeavoured to make us acquainted with the situation and history of the different countries of the world So wrote Gilbert the younger many years later My father had been a subscriber to Stackhouse s *History of the Bible* and from this Robert collected a complete knowledge of ancient history An uncle seeking a copy of *The Complete Letter Writer* obtained instead a small collection of letters by the *most eminent writers with a few sensible suggestions for* obtaining an easy epistolatory style This book was to Robert of the greatest consequence It inspired him with a strong desire to excel in letter writing while it furnished him with models by some of the finest writers in our language

My brother was about thirteen or fourteen when my father regretting that we wrote so ill sent us, week about during a summer quarter to the parish school that we might have an opportunity of remedying this defect ' In the next year we learn of the boys becoming acquainted with Fielding and Smollett with Hume and with books on English history In the following year their former tutor became English master at a nearby school and the elder brother revised his English grammar with his former master After a week the harvest intervened but he returned later for two weeks, during which time he learned French bringing home with him a French dictionary and grammar and the *Adventures of Telemachus* in the original In a little while by the assistance of these books, he had acquired such knowledge of the language as to read and understand any French author in prose This was considered as a sort of prodigy Acting on advice to try Latin in like fashion, he purchased the *Rudiments of the Latin Tongue* but finding this study dry and uninteresting it was quickly laid aside and this completes the account of his (Robert s) school education excepting one summer quarter some time afterwards that he attended the parish school of Kirkoswald to learn surveying

The father was William Burness (for so he spelt his name) a native of Kincardineshire The elder son Robert was born at Alloway in Ayrshire on Jan 25 1759

* * *

The *National Formulary* born by economics out of war has won a sure place in the doctor s bag ; and on the pharmacy shelf it stands in proud dilapidation beside the scarlet and gold *B P* in its fresh splendour Why isn t it fatter ? asks the doctor who hopes that it will prove a convenient source-book for most of his prescriptions. Why isn t it thinner? says the student— though he is likely to go on to grumble at the omission of radioactive isotopes I suspect that the Formulary Committee could have produced as many different formularies as there are county cricket clubs They must have known moments of anguish in deciding what to drop Preparations that they *have* dropped are listed in the new edition like loyal servants honourably retired and so doctors can catch by the coat tails an old friend on the way out, by writing, for instance, Solv Hydrarg Perchlor *N F* '52

The committee cannot hope to please everyone all the time But in its choice of pollarded Latin for titles of preparations it runs the risk of pleasing hardly anyone at any time Competent classicists will shudder at the hideous mutilation of a fine language, and the medical student will wonder why the committee cannot march in step with the compilers of the *B P* and *B P C* by opting for good plain English Anyhow, jubilation will be unconfined in the Potteries, whose craftsmen still make a whole range of receptacles embellished with the truncated Latin titles of obsolete Galenicals.

* * *

Our pooser hole was made to aid our latest cat whom we took because she was on the way to the gas chamber Our problems were the same as those of your correspondent last week, but now we have a two-way flap of hardboard which looks decorative and stands out at 45° with the slightest wind In cold weather the house gets icy We have had to increase the lagging on all the pipes and buy a special low-wattage anti-freezer for the water tank All is not on the debit side however, because when we bought our new puppy it was small enough to use the same hole Training was easy, but we are paying for it now because the hole is too small and the puppy won't bark to be let out She just sits in front of the hole on one side and because she can't get out won't let the cat in from the other

Our present problem is fairly simple—whether to spend the money on further insulation if we enlarge the hole or just wait and buy a new carpet later The cost seems to be about the same

* * *

Life in most hospitals passes quietly, and any minor departure from routine, such as the ejection of the residents' piano from an upstairs window, is liable to hit newspaper headlines Our latest claim to fame began with night sister's discovery of an unwanted man in the sluice For reasons still not quite clear, the resident obstetric officer was summoned to deal with her attendant vasomotor phenomena, and, since resident obstetricians tend to spring from a small-statured race, our colleague saw fit to bear a long stretcher-pole under his arm for protection Meanwhile the intruder had vanished without trace and the police decided to bring their bloodhound into action A large, sad-faced animal called Pluto was duly brought to the scene of the incident, but, overwhelmed by a host of new smells, he shook himself violently, chased his tail a few times, and made off in the direction of the labour ward where he barked loudly at a placenta lying in a bowl The commotion woke the babies in the nursery, who all started yelling at once Pluto took to instant flight and, after a careful search, was discovered ten minutes later in the grounds, digging a hole The sergeant who had long since despaired of finding the right scent, then announced that he would take the dog for one last frisk before retiring to the station This was a good cue for making some tea, and with Pluto contentedly munching an underdone sausage from the night-nurses' supper, a good time was had by all

* * *

The patient's complaint was worms—alleged to be three to six inches long and wriggling Suggestions for treatment were many Worm powders and drenches perhaps unreliable and difficult to administer Someone proposed waiting till night time when the worms come out, and then transfixing them or seizing them with dissecting-forceps He must have been a little mixed in his zoology, perhaps he was thinking of threadworms Another method considered was to bang on the surface with a hard object, the worms then come out to see what is going on, and can be grasped firmly This is too unkind to the patient The best suggestion so far is to send for a thrush This is not an example of one disease driving out another I forgot to mention that the patient is my lawn

* * *

‘ ector said ’e ’ad chain smoke breathing ”

# Letters to the Editor

## LEUKÆMIA AND ANKYLOSING

SIR,—A conference was recently convened Medical Research Council to consider new inquiring into the causes underlying the the death rate from leukæmia At this memorandum was presented drawing apparent association between leukæmia and spondylitis This information was based on limited number of instances, and the memb conference considered it very desirable th evidence should be collected on this possible association of leukæmia with ankylo litis is a curious one, but it may well be one that noted in individual patients by some of your

Dr W M Court-Brown, a member of the External Scientific Staff, at present working Department of Medicine, The Postgraduate School of London, Hammersmith Hospital, is collecting the relevant data on this subject. be very grateful if any of your readers who witnessed the occurrence of leukæmia in suffering from ankylosing spondylitis would him

Medical Research Council,
38, Old Queen Street,
London, S W 1

H P HIM

## MENTAL HEALTH AND PUBLIC HEA

SIR,—I welcome the fact that this subject raised in your leading article of Jan 15 It *not generally known that the curriculum for the* in public health as laid down by the General Council is no rigid set of rules and that men appears as part of both the preliminary and final the time which may be devoted to the subj left to the discretion of the teaching body which the course of instruction It is thus possible fo prehensive course in mental health *to be* this curriculum

In Edinburgh we do make a serious attempt of a series of lectures, demonstrations, and keep our students abreast of modern knowledge health and social aspects of mental health

I agree that “What is there to teach an an important question There is no room for co about what is already known concerning ment A substantial amount of what goes into is invalidated hypothesis, stimulating as a further research, but in itself not enough what is being done in other countries and much is now taught under the name of mental hygiene more than early treatment What is urgently is research into problems of prevention of mental who are the vulnerable members of the co how can they be found? and how can we help

These are the most important points, but have raised the question “Who is the proper visiting *and education in* a mental health I should like to comment on it The health by her vocation and early training as a sick general wards, quite unsuited for the task and training does little further to equip her to field of mental health The suggestion that she informed about these matters than the pub *doctor* is untrue for Edinburgh *and I* should be if it holds elsewhere In my opinion a more person for this type of work would be a social worker or an unspecialised social wor suitable supervision, but even their training improved for this purpose

Usher Institute
*Edinburgh 9*

DONALD CA

## TUBERCULOSIS IN IMMIGRANTS

Dr Doig's observations (Jan 15) on tuberculosis young people of the island of Lewis are most ng and I have no doubt that the high incidence culosis in Irish emigrants to England is also due minimal, undiscovered lesions which they take em, or to reinfection in England and not as d Macdonald[1] have suggested to any undue bility to infection Emigration from Ireland to the U.S.A Australia and New Zealand has ing on constantly since the end of the war and here have not been any reports of a similar e of tuberculosis there In order to be admitted countries it is necessary for one's lungs to be ically normal but tuberculin tests are not done would seem that if an Irishman has a normal ph of his chest at the time of emigration bility does not matter greatly

and Macdonald accepted the type of lesion in sh patients as evidence of recent primary infection rength of Wallgren's[2] time table of tuberculosis time table is applicable only to children and s it is rarely possible to decide the time of infection by studying the lesion alone

adults tend to develop relatively acute lesions pleural effusions and exudative infiltrations even if e been tuberculin positive since childhood Extreme of this phenomenon are described by Rich[3] who it that although the adult African typically contracts progressive type of disease which suggests a recent infection at necropsy evidence of healed childhood s very commonly found Another extreme example teration in the type of lesion which is a result of tivation. In Europe during the war acute tubercu the rule and this was related to the environment to the tuberculin state of the patients. On the and, Rich and others have shown that primary sis in the adult may be indistinguishable clinically reinfection type of disease My own experience of y district of Northern Ireland suggests that pro- primary tuberculosis in adults is extremely uncommon ems quite reasonable to suppose that the unfavourable ings in which Irish emigrants find themselves in are enough to account for the rather florid disease ey develop

k however that it is in their invocation of the miological phase of tuberculosis in Ireland that d Macdonald go most seriously astray

believe that because of later acquaintance with sis the rural Irish have less resistance to tuberculosis e English This argument is difficult to follow in those parts of Ireland where there is a high pro of negative tuberculin reactors there is a lower osis death rate than in Southern Ireland as a whole d Joyce[4] found in County Roscommon only 14·5% in positive at the age of 18 Admittedly only 69 of this age were tested and these are not representative e county but there would seem to be some indica many young adults there are susceptible to infection ative tuberculin reaction is taken as an index of ility Furthermore Flynn and Joyce assume (I am te correctly) that the number of tuberculin negatives sing from year to year; yet in 1943 the tuberculosis te in County Roscommon was 100 per 100 000 and it was 20 But apparently the epidemiological in 1943 was more favourable than 10 years later there were more positive tuberculin reactors in 1943 rate of 100 per 100 000 as recently as 1943 indicates y widespread tuberculous infection has existed in h countryside and it is impossible to see how a n by nearly 75% of this death rate in 10 years can stent with an increasing susceptibility to the disease ms fair to presume that the deaths in County Ros have followed the usual trend of a falling tuberculosis death rate towards the upper age groups. Yet at the age of 30+ Flynn and Joyce found that 66·6% were tuberculin positive although here again the number of persons tested was not an adequate sample It is most probable that in Roscommon deaths from tuberculosis are not *occurring in* the traditionally susceptible tuberculin negative young people but in the traditionally resistant tuberculin positive mature middle aged or elderly adults The same is true of all communities from which tuberculosis is receding There are large areas of the U.S.A where the tuberculosis death rate is negligible where scarcely any of the children or young adults are tuberculin positive and where the deaths are mainly among *the elderly* who having spent their childhood in a time when tuberculosis was prevalent are the most likely to have been exposed to infection early in their lives Conversely in populations with high tuberculosis death rates there is always a high proportion of positive reactors, and a high reactor rate in children is always associated with a high death rate in young adults. It is wise to remember that no community has yet controlled tuberculosis by tuberculinisation of its members In any country where 100% of the people are tuberculin positive it can be guaranteed that tuberculosis will be the most important cause of death

It seems to me that the 'virgin soil theory of tuberculosis is plausible but quite fallacious and unable to withstand critical analysis Destructive tuberculosis is a disease of tuberculin positive people and acquired resistance while it may influence the course of the disease in individual patients does not seem to exert any significant effect in preventing new cases We must face this fact if we are ever to resolve the vast perplexity of the immunology of tuberculosis

Dungannon Chest Hospital
co Tyrone Northern Ireland

F F JAMES

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[1] E. V Macdonald N *Lancet* 1951 ii 13
[2] gren A *Tubercle* 1948 29 243
[3] A R. Pathogenesis of Tuberculosis. Oxford 1951
[4] n M I Joyce J C *Tubercl* 1951 35 90

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## IMPOTENCE

SIR —Dr Tuthill (Jan. 15) seems to me to deserve great credit for putting forward an original logical and therapeutically valuable way of looking at cases of impotence I do not see cases of impotence but it is one of a group of conditions such as enuresis in which physiological pathological and psychological mechanisms are interwoven Of the last physiological and pathological superficial and deep primary and secondary factors are often difficult to sort out It is often necessary to explore some way along physical lines then for simple psychological causes returning if necessary to look for rarer physical causes and then again returning if need be to look for deeper psychological causes Some of the patients who failed to reply to Dr Tuthill's questionary may well have needed deeper investigation but he has shown that approaching the problem physiologically often gives speedy and lasting help It would be of interest to hear the views of others with experience of treating dyspareunia and the results of their methods and it is also to be hoped that Dr Tuthill will report on the results of a similar fresh approach to dyspareunia and frigidity

London S W 1

RONALD MAC KEITH

SIR —It was interesting to read Dr Tuthill's paper on impotence and few would disagree with some of his views It was rather surprising however that a psychiatrist should decry psychological methods of treatment and praise the use of male hormone for which he claims success Most endocrinologists would confirm the statement that testosterone is not helpful in cases of functional impotence and it has been my experience that common sense psychiatry is often adequate

If erectile capacity is not a constant but is reduced by stress, worry, or failure" why should small doses of exogenous testosterone increase it?

Erection is partly dependent on male hormone secretion from the testes but can occur without it For example a eunuchoid patient aged 34 with primary testicular agenesis and the penile development of a prepubertal boy was able to have intercourse regularly with his wife before he was developed maturely by testosterone therapy

An adult normal male whom I saw after his metamorphosis into a pseudo female had been treated with large doses of œstrogen for two years He told me that he was able to obtain rigid erection and his potency still persisted when his testicles were removed Even when a plastic surgeon had divided the corpora cavernosa, which were built into the form of labia, painful priapism necessitated their later amputation

Dr Tuthill's case records tell us nothing of the state of the gonads of his patients If these were normal, then presumably there was no reason why male hormone should not be secreted in adequate amounts

I hesitate to comment on the inefficacy of oral methyl testosterone therapy in such cases An implant of 100–200 mg testosterone in 25 mg tablets would possibly last some months with the daily absorption of a few milligrammes at first *In several cases of functional impotence with normal gonads,* judged clinically and by testicular biopsy, I have administered doses of 300 mg of testosterone phenylpropionate or testosterone isobutyrate twice weekly without any significant effect over periods of some weeks

Let us hope that the proprietary pill containing amphetamine *sulphate, strychnine, arsenic, and yohimbine is* categorised in group 6 of the Standing Joint Committee's classification of proprietary medicines I thought that yohimbine, like *cantharidin, was no longer fashionable as an aphrodisiac,* and in fact I have yet to hear of any drug which has been proved to have this power in the normally developed male

I feel that Dr Tuthill is too modest and that his records of successful hormone treatment of erectile impotence are really a tribute to his psychiatric technique and experience

Bristol G L FOSS

SIR,—Dr Tuthill's article is valuable for the encouragement it gives us to use simple adjustment, rational counsel, and physical therapy Yet as regards treatment it leaves us largely in the air Treatment seems to consist in advising the abandonment of restraint and prescribing endocrine therapy as a reinforcement One is reminded of the adage that cases of impotence are either very easy or very difficult to treat, and perhaps Dr Tuthill has not ony re discovered this fact, but has added to it counsel of value—namely, that we should adopt simple reassurance on rational lines before more disturbing techniques are considered Unfortunately he has too little to say about the difficult cases His comment on sex fantasies deserves consideration, and the whole paper is a worthy contribution to the literature on this subject The scorn with which he regards medical psychologists—men as sincere as he—is regrettable

St George s Hospital,
Hornchurch, Essex D T MACLAY

## "TAKE A COUPLE OF FAT VIPERS"

SIR,—A critical mind was possessed by the anonymous author of the second edition of the *New Dispensatory,* published in London in 1746 In discussing the relative advantages of live and dried vipers in making vinum viperinum, he writes

> "Whether they communicate to the wine, either when used fresh or dry, so much virtue as they are supposed to do, is greatly to be doubted Some compositions under this name have been highly celebrated, as restoratives in debilities and decays of constitution, but what virtues of this kind they possessed, were supplied chiefly from other ingredients
>
> The viper is doubtless highly nutritious food, and in some kinds of weakness and emaciated habits, is not undeservedly looked upon as a good restorative To answer any valuable purpose, fresh vigorous vipers (not such as have been long kept alive after they are caught) should be liberally used as food the wines and tinctures from them can scarce be supposed to receive any considerable virtue from the animal, the dry flesh brought us from abroad is entirely insignificant'

This dispensatory describes the preparation of Theriaca Andromachi or Venice Treacle, one of the electuaries 'of wild exuberance of composition which the superstition of ages brought into vogue,' and lists 61 ingredients

It is interesting to learn from it that, while the College have somewhat facilitated the preparat medicines by omitting the hydeclroi and dried vipe College of Edinburgh, paying very little deference t or common prejudice, have ventured at length t these venerable reliques"

The Royal Hospital
Sheffield 1 PETER

## INTRAVENOUS HYDROCORTISON

SIR,—Hospitals holding stocks of corticotro cortisone have now received from the Ministr a small supply of hydrocortisone solution fo intravenous administration Until recently of this preparation has been available in th and few reports have been published about i May, 1953, the Medical Research Council made 1 2 g of an aqueous suspension of hydrocort alcohol (Merck), and after preparation by the described by Thorn et al [1] this was used infusion Certain practical details in the use venous hydrocortisone have been emphasised by experience and may be of value to others who able to use this new preparation

*Adrenal cortical Insufficiency*

In severe adrenal cortical insufficiency the firs treatment is to raise the level of circulating adren hormone If the patient is conscious and able to medication, cortisone tablets will produce a significa of the plasma 17 hydroxycorticosteroids in thirty minutes [2] If treatment by mouth is impossible, cortisone is of limited value because of its very slow rate Hitherto the only preparation capable of rapid increase of circulating hormone has bee cortical extract given intravenously Solutions cortisone are much more potent and likely adrenal cortical extracts for use in emergency

Severe adrenal cortical insufficiency requiring therapy may take the form of an addisonian cris develops gradually, depletion of sodium and fluid play an important part in the production of When treating a case of this type the concentrated hydrocortisone (100 mg in 20 ml 50% alcohol) added to 1 litre of physiological saline

On the other hand studies have shown that rapi ing adrenal insufficiency can quickly result in tension without any external loss of body practice this may arise in the course of adrenal patient with Addison's disease or cortisone-indu atrophy is subjected to a severe stress and possibly adrenal hæmorrhage In these cases there is depletion, and the hydrocortisone should be given glucose solution

Two cases of addisonian crisis have been tr intravenous hydrocortisone Both were of the slow ing type, one due to inadequate replacement th adrenalectomised hypertensive with impaired renal and the other in a previously undiagnosed case of disease The hydrocortisone had been prepared adrenal surgery and was therefore made up in isotc solution Furthermore, so that the clinical and b effects of the infusion could be studied, no other ster was given during the infusion or for some hours The results were disappointing, although there wa clinical improvement the effect soon disappeared patient with renal insufficiency the blood urea potassium levels rose Both patients responded to additional salt and oral and intramuscular

The poor response of these two patients may be to giving the hydrocortisone in isotonic glucose saline solution and to the fact that no additi therapy was given at the same time Hellman shown that hydrocortisone disappears from the very quickly after the completion of an infusion

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1 Thorn G W Jenkins D, McCracken B H,
J A Reddy, W J *Trans Ass Amer Physns*
2 Nelson, D H Sandberg A A Palmer, J G,
*J clin Invest* 1952 31, 843
3 Pearson O H Hollander V P West, C D Whit
Randall H T *Ibid,* p 653
4 Hellman L Bradlow, H L Adesman J Fukush
Kulp J L Gallagher T F *Ibid,* 1954, 33, 11

xperience with these two patients we suggest that travenous hydrocortisone is used for the treatment of f addisonian crisis it should be given in isotonic saline and that injections of cortisone acetate should be ur hourly in the initial stages. Cortisone acetate by should be started as soon as possible Thorn et al [4] ggested that the intravenous hydrocortisone should at a rate of 25 mg per hour for the first two hours mg per hour subsequently; they also advise giving of deoxycortone intramuscularly in patients with a sma potassium level

patients developed acute adrenal insufficiency shortly eration. One patient had had a total adrenalectomy hing s syndrome; and although she had received of cortisone intramuscularly in the previous twenty urs, profound hypotension developed twelve hours eration An intravenous infusion of hydrocortisone in lucose solution at a rate of 12 5 mg per hour produ ediate and dramatic response The second patient cortisone therapy for two months before splenectomy dertaken for hæmolytic anæmia It was anticipated e patient s adrenals would be atrophic and unable to to the stress of surgery therefore 350 mg of intra r cortisone was given in the twenty four hours before ration. A further 150 mg was given in the next hours, but fourteen hours after operation there was fall of blood pressure Intravenous hydrocortisone in glucose was given Initially the rate was 6 mg per d the blood pressure moderately improved when the increased to 12 mg per hour it returned to normal.

*ative Shock*

et al [6] reported good results from intravenous hydro o given for the treatment of severe postoperative the absence of any evidence of adrenal insufficiency e two infusions to one patient in this condition but there was slight improvement it was not maintained patient ultimately died

is

se of intravenous hydrocortisone as a diagnostic test rentiating between tumour and hyperplasia in cases of s syndrome or adrenogenital syndrome was described r et al.[7] If effective it would have the advantage of uch quicker as a diagnostic procedure than the usual scular cortisone suppression test We obtained a ical result from this test in a case of Cushing s syn Although an infusion of 100 mg of hydrocortisone ver four hours failed to reduce the 17 ketosteroid no tumour was found at operation.

l account of these studies will be published in the sue of the *Archives of the Middlesex Hospital*

de of Clinical Research
Middlesex Hospital
London, W 1

JOHN NABARRO

## HEXAMETHONIUM AND THE PUPIL

—Several years ago while using hexamethonium e in the investigation of the vasomotor reactions ents suffering from poliomyelitis I noticed some ing changes in the pupillary reactions of these s. The changes included bilaterally equal mydri miosis, anisocoria isolated loss of the pupillary o light isolated diminution of the pupillary reflex ergence-accommodation and loss or diminution h the light and convergence accommodation

patients who received intramuscular injections of 40– of hexamethonium bromide 3 showed an isolated l loss of the light reflex 3 showed a sluggish con e-accommodation reflex while the light reflex remained nd 3 showed sluggishness of both reflexes 4 of the 9 had an equal mydriasis 3 had a marked anisocoria ad no change in pupil size

ould be interesting to know if there have been any l investigations of the effects of ganglion blocking agents on the pupillary reflexes—for example the injection of a blocking agent in graded doses into the internal carotid or ophthalmic arteries Such an investigation particularly by close arterial injection into the ciliary ganglion might throw some light on the mechanism of the Argyll Robertson pupil

Hoddesdon Herts

A McPHERSON

## SEX OF MEDIASTINAL TERATOMATA

SIR —Following on the recent observations on sexing by means of nuclear characteristics, and more particularly on the findings by Hunter and Lennox [1] in relation to the sexing of teratomata it was decided to ' skin sex ' our small collection of mediastinal teratomata The sections were reviewed and five cases selected in which reasonable areas of squamous-cell formations were found For controls skin biopsies were taken from six known males and six known females. The findings were as follows

| *Patient* | | *Teratoma* | |
|---|---|---|---|
| *Age at operation* | *Sex* | *" Skin sex "* | *Position* |
| 1 yr | M | F | Anterior |
| 18 yr | M | M | Posterior |
| 1 yr | M | M | Anterior |
| 7 days | F | F | Anterior |
| 24 yr | F | F | Thymic |

Having found one apparently contra sexed teratomata in the series I approached Dr Lennox, who kindly agreed to re-examine the material, provided that all indication of sex was withheld until his examinations were complete His findings fully confirmed mine and he was confident of the accuracy of the sexing in the case of the contra-sexed teratoma

The only comment I would make is in relation to the discussion in the paper by Hunter and Lennox [1] In males the proportion of XX, XY and YY zygotes should be 1 2 : 1 Clearly the heretical supermale YY is a potential novelty and the investigation of two questions may produce additional evidence : (1) does the proportion of female teratomata in males approach $^1/_4$ or $^1/_2$ as the statistical limit ? (2) is there a chromatin pattern characteristic of the (assumed) YY zygote ?

Sims Woodhead Memorial
Laboratory Papworth
Hospital Cambridge

D BARRON CRUICKSHANK

## HARDENED FATS AND LUNG CANCER

SIR,—Professor Yudkin in his letter of Jan 1 claims that deficiency of essential fatty acids has never been shown definitely to occur in man But Burr [2] has referred to the study of eczematous patients in whom the blood level of both arachidonic and linoleic acid was lower than normal ; and he added Although the results with human subjects are not so uniform as those with experimental animals under controlled conditions it seems clear that many people are receiving less than their optimal requirement of linoleic acid. He also mentioned that an adult maintained for six months on a diet which produced deficiency symptoms in young rats felt no ill effect but he lost weight underwent a change in respiratory metabolism and suffered a marked drop in the arachidonic and linoleic acid content of the serum lipids

It is well known that hydrogenation of fats eliminates essential fatty acids and that the hardened fats so produced are used in margarine and other foods That does not mean that these foods are free from essential fatty acids but only that an increased consumption of these foods reduces the content of essential fatty acids in the diet Burr said :

> From a survey of the national dietary it has been estimated that linoleic acid constitutes 1% of the average American s food It is likely that many people consume less than this amount which has been suggested by some as the

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G W Jenkins D Laidlaw, J C Goetz F C, Blumman, Aron W L, Streeten D H J, McCracken B H Engl J Med 1953 248 281

J M, Orr R H Forsham P H Metabolism 1954 81

J W, Gold J J, Wallace L Z Amer J Med 1951 310.

[1] Hunter W F Lennox B. *Lancet* 1954 ii, 633

[2] Burr G O *In* Dietotherapy edited by M G Wohl Philadelphia 1945 pp. 4 5 80

amount required by rats It is not surprising, therefore, that there are individuals who, because of low intake or abnormally high requirement, respond to additional unsaturated fatty acids in their diet "

Lung cancer varies between town and country and from province to province, and so does diet A comparison only between whole countries, such as Professor Yudkin makes, cannot therefore tell us much The relatively low prevalence of lung cancer in females may be connected with the fact that female laboratory animals require less essential acids than males

Copenhagen JOHAN NYROP

## STRANGE LANGUAGES

SIR,—I feel somewhat diffident in replying to Dr Wayne's inquiry in your issue of Jan 1 , but may I point out that a *Polyglot Medical Questionnaire* in twelve languages was published by H K Lewis & Co two years ago? It depends, of course, what he means by " strange languages," but I think he might find this book helpful —especially if he is working in dockland It contains both popular and medical terms and the translations have been done by doctors who speak English as well as their own tongue

Droxford Hampshire S CHALMERS PARRY

## CHEMOTHERAPY OF LEPROSY

SIR,—Dr Jopling's letter (Jan 8), pointing out that results of sulphone treatment of leprosy in England are less favourable than I had found in Nigeria,[1] emphasises a point I myself made in the article in question I discussed the less favourable reports made also in the U S A , since no published reports were available for this country It appears possible that a racial factor influences the severity of leprosy and the results of treatment

As Dr Jopling surmises, I do not say that all is well with the treatment of leprosy , but I, and all other workers I know, do say that all is infinitely better than it was before sulphone treatment was introduced If I were completely satisfied with sulphone treatment, I should not have spent years on experimentation with the other chemotherapeutic agents mentioned in my article

I would discuss briefly three points

Firstly, in spite of what Dr Jopling writes, sulphone treatment of leprosy in England can give excellent results Although, through having been long abroad, my knowledge of leprosy patients in this country is very limited, I know of a few (though there must be more) English persons who, thanks to sulphone treatment, have fully recovered from lepromatous leprosy and are now living normal lives with no disabilities or deformities

Secondly, Dr Jopling's surmise that my patients in East Nigeria were easily cured because the disease had been rendered mild by the " clan segregation instituted some 20 or more years ago " does not bear examination When I arrived in Nigeria in December, 1947, I found in the Uzuakoli area about 12,000 patients under treatment and a degree of isolation at the Uzuakoli Settlement and its fifty outstations, under Dr T F Davey For our experiments with chemotherapy, to begin with we chose and treated in the one centre about 200 of the worst of these 12,000 cases, and particularly those which had become steadily worse despite many years of treatment with hydnocarpus oil With these patients we had many difficulties such as Dr Jopling describes and we described in previous articles , but in time the difficulties were overcome and cure was obtained, as recorded in my recent article During the next few years we gradually collected for special study another 900 highly active but newly diagnosed cases with no previous treatment, many of them from areas where there was no organised clan segregation In these cases the difficulties were very much less, and slow recovery is being seen in practically all of them

Finally, my experience is that with prompt diagnosis and early treatment, most of the complications mentioned by Dr Jopling do not often arise or are not serious I strongly suspect that in this country, for a variety of reasons, patients have not come under effective treatment soon enough to complications of treatment, which can be so which do subside in time We certainly found th Nigerian patients, with their early recognition of their determination to get better and to contin in spite of difficulties, we were fortunate in hav material to work with

It is possible, as I have already suggested, th factor helped us , but, even so, the results m such a large scale in a country where leprosy problem, do justify the opinion that a major in treatment has occurred , and I should li acknowledge our indebtedness to the workers nations—particularly German, French, and well as British—who contributed to this revolu

British Empire Leprosy Relief Association, JOHN L
8, Portman Street, London, W 1 Medical

## SULPHONAMIDE SENSITIVITY OR DISSEMINATED LUPUS?

SIR,—Dr Fox rejected the diagnosis of dis lupus erythematosus, in the case which he re your issue of Jan 22, on the ground of a single marrow examination, done one month after th had lost her fever Had this examination been during the pyrexial period lupus erythemato still have been the most likely diagnosis The sex of the patient, the previous œdema of the onset in summer at the seaside, the malaise, p pyrexia, the morphology and distribution of the the rapid sedimentation rate, the loss of hair, tedious illness all point to disseminated lupus er tosus This is more than an academic point prognosis is serious

The sulphonamide may have activated the but it is not justifiable to regard this as a case sulphonamide sensitivity In disseminated lupus matosus a peculiar type of hypersensitivity for an unknown cause, spontaneously Attacks precipitated by exposure to sunlight or the ing sulphonamides

Edinburgh 12 ALAN L

## MASKED EPILEPSY

SIR,—Dr Kempton (Jan 22) tries to hoist my own petard He accuses me of ascribing every to one cause—epilepsy If he read my paper he would find that the 7 cases were drawn from 1400 patients and that I recommended a investigation to exclude other causes of the In the *British Medical Journal* of Jan 15 I h thirteen causes of abdominal pain in addition to lous mesenteric adenitis Dr Kempton prefer to the term "periodic syndrome," which he provisional He asks whether a diagnosis of is of benefit to anyone The answer is that later a child with periodic pain will become a unnecessary abdominal operation, as described in America More important is the fact that one of the patients will have a severe and attack from which he will not recover Such a reported by Brown[1] If we can prevent only these tragedies then it is worth all the "d social implications" of revealing the true the parents In my experience parents are sensible and only too pleased to have a rationale tion of a disease which has obviously puzzled their advisers They are even more grateful it cured

Dr Scott asks about toxic effects of pheno In case 7 the drug reduced the incidence of but made it more severe when it did occur Th what happens with grand mal sometimes I noticed any behaviour disorders or irritability cases these complaints were relieved by pheno e.

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[1] Lowe J *Lancet* 1954 ii 1065

[1] Brown R J K *Brit med J* 1954, ii, 105

r annotation of Jan. 8 you say that the choice rm masked epilepsy ' is perhaps unfortunate in that it is simple and expressive The comment was used when the electro encephalographic vas less well defined does not alter the fact that cases epilepsy wears a mask and is therefore ised It is unrecognised by the parents, by the octor and by the consultant (including myself irst saw cases 5 and 6) An eminent neurologist hes to remain anonymous has written to me to in his large experience he has seen very few d he considers the condition to be very rare the penalties of living on an eminence is that not see in detail what goes on at lower levels no reason why these cases should ever come to ce of a consultant in neurology Their fate is en to have their appendices removed to be told e is nothing the matter with them or to be classed g abdominal pain of unknown origin Occasion esperation the family doctor gives them pheno e, considering it to be a universal sedative es them, and everyone is happy They are still from masked epilepsy though no-one ever Is this an adequate reason for abandoning a hich was good enough for Sir Frederic Still? ternative, visceral epilepsy is not quite so nt for it can hardly be considered to cover such ations as night terrors, sleep walking and odd r

HUGH R E WALLIS

## OCCUPATIONAL HEALTH SERVICE

May I express my regret to your correspondents delay in replying to their letters.

o who for some ten years served in the oldest st comprehensive occupational health service in try—namely that of the Royal Navy—I fully te the necessity for clinical experience and close with every aspect of the work to be undertaken knowledged foundation of that occupational rvice is preventive medicine

me will require the answers to questions of relative h regard to the health hazards of occupation.

physician in occupational health is to supply the he must have the necessary information available t available he must obtain it The study of such data l to occupation inevitably becomes occupational logy Let those who reject the claims of the epidemio- comment in the field of occupation consider the re which will be the appointment of a lay assessor ta accumulated by the creation of a comprehensive If the clinicians wish to argue with a lay administra- he trade unions or the employers do they consider medical data should be handled by medical men or n? Someone will have to comment in an informed n the over-all situation particularly when after the usastic setting up of an occupational health service nistration having overreached themselves in extrava nses, lay the chill hand of economy on the service the time for the full evidence of real need to be

vor Lane[1] appears to be unable to distinguish industrial *medicine* and occupational *health* posed service is an occupational health service cupations have no relation to the factory For female hairdressing is said to be the second women s occupation Delivery rounds the ndustry the building trades catering office work ice work—these occupations have no link with omium plated factory surgeries which appear so ideal for some In replying to the query of r Lane as to what medical officers of health have done for occupational health I would refer him to the information in his own social medicine unit and say that in the vast occupations of being an *infant*, of *being a school-child*, of being a mother and of being an old person preventive medicine has improved *health standards* beyond all knowledge in the past hundred years The same preventive health outlook is necessary during the forty hours or so each week in which the adult earns his living to support himself during the remainder of his waking and his sleeping hours

Health Department,
Brighton.

W S PARKER
Medical Officer of Health.

## TUMOURS OF THE GLOMUS JUGULARE

SIR —An interesting point arises from Dr Holesh s paper of Jan 22 Cell nests resembling the glomus caroticum, are found not only at the bifurcation of the common carotid artery but also in the adventitia of the ascending aorta its arch or in the innominate artery in the ganglion nodosum of the vagus nerve in the adventitia of the jugular bulb or along the course of the tympanic nerve (glomus jugulare) and in chimpanzees they have been discovered in the orbit in relation to the ciliary ganglion[1] Tumours arising from each of these sites have now been described[2]—excepting the orbit One of our series of patients with glomus jugulare tumours[3] had a very marked proptosis and at necropsy the tumour was seen to lie in the orbit but it appeared to have invaded it by extension forwards from the petrous area rather than to have originated there.

Dr Holesh s case 4 however also showed a proptosis, but some years before any of the other signs developed and in view of the well known tendency for the glomus tumours to form concurrently in two or more sites, it seems worth considering the possibility that the original site of tumour formation in this case might have been the orbit and that this type of tumour might be included in the differential diagnosis of causes of unilateral exophthalmos

Another feature in the diagnosis of these tumours is their tendency to present as a tongue of tumour inside the lumen of the jugular vein and to be found as a pulsating swelling having a palpable thrill and audible bruit under the lobe of the ear between the mastoid and the jaw This was most marked in 1 of our series[3] and in 2 of the cases of Henson et al[4] and it has occurred in just under 10% of all reported cases

Midland Centre for
Neurosurgery
Birmingham, 41

EDWIN R BICKERSTAFF

## *HEARING TESTS*

SIR —I should be grateful if you would give me an opportunity of replying to the letter from Miss Whetnall in your issue of Jan 15 The title of the statement to which she refers and which you were good enough to publish for the Medical Research Council on Jan 1 was The Sweep frequency Method of Making Screening Tests of the Hearing of School-children The council did not ask me to draft a comprehensive statement on the ascertainment of defective hearing in childhood The sweep frequency method was recommended in my statement and with the council s authority for use by school medical officers in detecting defects of hearing among children which have escaped ascertainment during their pre school life or have occurred without having been otherwise ascertained after their admission to school

With financial support from the Medical Research Council a clinic in which special provision is made for testing hearing in infancy and early childhood was

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[1] Lane R. E. *Lancet*, 1951 ii, 13 9

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[1] Lattes R Waltner J G *Cancer* N Y 1949 2 44

[2] Lattes R *Ibid* 1950 3 667

[3] Bickerstaff E R Howell J S *Brain* 1953 76 76

[4] Henson, R. A., Crawford J V Cavanagh J B *J Neurol Psychiat* 1953 16 1 7

established by the University of Manchester in this department in 1934 This research unit appears to have been the first of its kind, and the procedures that my wife and I have evolved for testing the hearing of children aged 3 months to 5 years have been reported in the *Journal of Laryngology and Otology* and in our books

In a recent report on *The Health of the School Child* the chief medical officer of the Ministry of Education has been good enough to refer in some detail, and very favourably, to my wife's work in training health visitors to test the hearing of children at maternity and child welfare clinics, under the supervision of medical officers My wife has found health visitors to be very suitable for this work In the cities of Birmingham, Leicester, and Salford, and in Lancashire, Leicestershire, and Northamptonshire, screening tests have already been begun of the hearing of all children who are brought to maternity and child-welfare clinics With my wife's help a growing number of health authorities are establishing guidance clinics for the parents of children who have been found to be handicapped by deafness (which is not amenable to medical or surgical treatment) and who have not started school

A collaborative project, for the further study of deafness in childhood, in which senior members of the staffs of the departments of otolaryngology and education of the deaf, in this university, are taking part, is at present in progress

Department of Education of the Deaf,
The University, Manchester

A W G EWING

## ARTIFICIAL HIBERNATION IN POLIOMYELITIS

SIR,—In your issue of Jan 15 Dr Brehme states that in bulbar respiratory paralysis chlorpromazine would, by lowering the basal metabolic rate, decrease oxygen consumption and so lessen the risk of anoxæmia Although it was at first thought that chlorpromazine decreased oxygen consumption, later work has in fact shown that this drug slightly increases oxygen consumption For this reason, and to avoid the tachycardia which chlorpromazine produces, I have used 'Hydergine' (which contains the methanesulphonates of the three alkaloids dihydroergocornine, dihydroergocrystine, and dihydroergokryptine in equal proportions) in lieu of the chlorpromazine constituent in the lytic cocktail Like chlorpromazine, however, hydergine can produce profound hypotension when given intravenously

Hull

W N, ROLLASON

## NOTES ON TRANSFUSION

SIR,—"Clinical Pathologist" (Jan 22) is to be sympathised with in his concern to prevent the wasting of blood that has been cross-matched but then not required, and a more realistic approach to the problem by the Ministry is desired

In the first place, pathologists and technicians worth the names are capable of breaching sterile containers without admitting infection—that simple procedure is part of their training, and without it no culture of any sort could be put up in the bacteriology department

In the second place, it is urged that those of us who cross-match blood should stain a film of a sample of each bottle by Gram's method as part of the essential technique This at once removes any value of a pilot tube as only the blood in the pint bottle matters in the examination for organisms Thus the bottle must be breached Why then go to the expense of fitting pilot tubes ?

Either a pilot tube to prevent repeated bottle punctures or the staining of a film for bacteria is desirable Both together are incongruous—and incongruity is what we try to avoid in cross-matching blood !

[illegible] Hospital

C A K BIRD

SIR,—Reading through the correspondence columns, an onlooker must come to the con does Clinical Pathologist in his letter last several important problems would be solved universal introduction of pilot tubes

I have been *expecting to see an* putting forward the objections to pilot tubes been said that pilot tubes are objectionable the danger of switching these tubes either at the session or subsequently, and also because the inside the main bottle may be infected or dam the pilot-tube blood remains unchanged The the blood in the main bottle was dangerous go undetected at the time of cross match Th would seem to be small, and it would be helpful if we could learn whether the experts that such risks can reasonably be disregarded.

ANOTHER CLINICAL PA

## WATER DIURESIS IN PRIMARY M

SIR,—Both the recent article by Dr Hubble and the letter from Dr Fraser and Dr Garrod that failure of water diuresis is not uncommon myxœdema

Hubble cites Crispell et al [2] as supporting this et al believe that there is failure of water diures myxœdema , but detailed analysis shows that, of their patients had a poor diuresis compared people, only 3 cases of the 11 had a failure of of the kind seen in adrenal deficiency Garrod and found that in 16 out of 18 patients with the rate of urine flow and the proportion of excreted were very different from the results in patients with hypopituitarism Levy et al [4] found water diuresis in all 3 cases of primary myxœdema studied.

RESULTS OF WATER DIURESIS TEST (1 LITRE INGESTED) IN 9 CASES OF PRIMARY

| Case no | Sex | Ætiology | Max rate of urine flow (ml per min ) | Proportion of load excreted |
|---|---|---|---|---|
| 22 | M | Idiopathic | 6 8 | 100 % in 3½ hr |
| 26 | M | Surgical | 8 4 | 80 % in 3½ hr |
| 30 | F | Surgery and X ray | 6 0 | 66 % in 4 hr |
| 38 | F | Surgical | 11 0 | 94 % in 4 hr |
| 39 | M | Idiopathic | 3 3 | 55 % in 3½ hr |
| *40 | F | Idiopathic | 6 3 | 84 % in 3½ hr |
| 41 | F | Idiopathic | 6 0 | 65 % in 4 hr |
| 42 | F | Idiopathic | 7 0 | 100 % in 4 hr |
| 43 | F | Idiopathic | 2 5 | 33 % in 3½ hr |

* This patient had thyroid extract gr 1 per day for the test

The accompanying table shows the results of diuresis tests in 9 cases of primary myxœd technique used, and the results in cases 22 and already been reported [5] In 7 out of the 9 cases diuresis was normal In 1 (case 39) of the there was concomitant heart-failure, and, known, patients with heart failure due to have a failure of water diuresis

I still believe that the water-diuresis test valuable in distinguishing primary myxœd myxœdema secondary to hypopituitarism patients with primary myxœdema have a water diuresis of the kind seen in hypop and in this event cortisone will not produce

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1 Fraser, R. Garrod, O *Lancet*, 1954, ii, 919
2 Crispell K R Parson W , Sprinkle, P *J* 1954 14 640
3 Garrod, O Gilliland I C *Proc R Soc. Med* 195
4 Levy, M S Power M H , Kepler E J *J* 1946, 6, 607
5 Oleesky, S *Lancet*, 1953, i 769

as it usually does in hypopituitarism Thus patient with myxœdema has failure of water then pituitary failure must be considered as the cause of the myxœdema This is important dministration of thyroid alone to a patient with ma secondary to hypopituitarism may occasion uce an adrenal crisis

ll Hospital
chester

S OLEESKY

## CANCER OF THE LARYNX

I was interested to read Dr Maxwell's article x on the incidence of cancer of the larynx in o the incidence of cancer of the bronchi

ve he has made a fundamental error in drawing lusion that it is now certain that cancer of ax has not increased in frequency during the iod in which cancer of the bronchi and lungs me very much more common His conclusion on the Registrar General's figures for deaths se diseases over a period of years

of the larynx is a superficial form of cancer or the fact that it reacts favourably to adequate t—surgery or irradiation or a combination of very experienced laryngologist has cases which n followed up for many years and in which no recurrence though the patient may die of er disease On the other hand cancer of the eneral does not respond to treatment which is arely palliative

egistrar General's figures for deaths from cancer ing accurately reflect its incidence but the r deaths from cancer of the larynx relate only to or untreated case or the case that has not d to treatment and they do not, in my opinion ue picture of the extent of cancer of the larynx his disease is probably also on the increase

er Royal Infirmary
Doncaster

PHILIP H BEALES

## INSECTICIDAL LACQUER

In your annotation of Oct 9 you estimated that cost £50 to apply insecticidal lacquer to a kitchen and £5 to treat a ward kitchen You aid that 'the lacquer has to be applied by and the cost is high though perhaps not in view of the long term benefit.

gard all these statements as incorrect. In the the cost should not be nearly as high as stated lthough of course the actual cost will vary to the size of the kitchen Secondly insecticidal suitable for use by any energetic person One ntains sufficient to treat *80–100 square yards* not necessary to treat the whole surface but int strips, 4–6 inches wide along edges crevices t haunts.

employment of a technical disinfestation service l committee make use of expert knowledge and e as well as qualified operators and for this e to pay In many cases it may be decided is well worth the extra expense involved. None we feel that your annotation presented a false your readers since where the hospital decides the material with its own personnel it should be ut those costs by at least 50% Under these nces we have no doubt that the use of insecticidal will be a more attractive proposition to your

METALLURGICAL CHEMISTS LIMITED

Broad Street
on, E.C.2

r estimate for treating a hospital kitchen was from a servicing company and we understand director of the company had in mind a very large kitchen In such jobs as in the building industry generally the cost of skilled labour is often much greater than that of the materials themselves. Our opinion that insecticidal lacquer should be applied by experts was based first on the need to mix it immediately before use with an accelerator containing 10% sulphuric acid and secondly on the precautions that have to be taken during application (For example in telling people how to use their product Kyplaq our correspondents say Do not inhale vapours Ensure maximum ventilation Do not expose naked lights during application or for 3 hrs afterwards Wash hands and face with soap and water after applying Do not overpaint or the actions of the insecticides will be impeded ) Thirdly the best results will be obtained by someone who knows the haunts of the insects and what kinds of surface are most suitable for treatment —ED L

## TOO MANY ANTIPYRETICS?

SIR,—At a time of the year when influenza and acute coryza are all too common it is pertinent I think to inquire again on what grounds the very widespread use of antipyretics is based

Not only do the public flock to buy many millions of bottles of tablets of various mixtures containing salicylates but the main aim of many practitioners appears to be to promote diaphoresis and to lower that raised body temperature at all costs—in other words to get their patients to sweat it out Of course most of these mixtures and the time honoured Dover's powder are analgesics but it is the antipyretic side of their action which I maintain is irrational

On more than one occasion I have allowed my own pyrexia to deal with the invading pathogens and it has coped pretty well. I do indeed endorse the statement[1] that the reduction of temperature is rarely indicated '

London S E 9

N P BRONSDON

## ISOBEL CRIPPS CENTRE

Dr B Courtenay Mayers writes

May I as medical adviser to this centre, correct the unfortunate impression given by Dr Barlow (Jan 15)? Every *possible safeguard is being taken by Mr Neil and his colleagues.* I myself have seen many of Mr Neil's pupils, who have not been under other medical care and I know that other doctors have too I have every confidence in Mr Neil's work and provided suitable cases are chosen—i e cases where poor posture malcoördinated movement or undue tension play a significant part—then very good results can be obtained I am surprised that Dr Barlow should confuse Mr Neil's case with that of the osteopaths: to do so is to say the least of it, highly misleading

Dr Wilfred Barlow writes

For several years Mr Neil has carried out an intensive advertising campaign in the national press In several of these advertisements he cites medical conditions—e g., A method of proved value in many states of physical ill health and psychological disorder One advertisement tells people to *Ask Your Doctor about his school* and this to the layman might easily imply general medical support It seems to me meaningless to talk about being ethical after one has advertised in this way however zealous one may then be in contacting the doctors whose patients have come as a result of the advertising The fact that Mr Neil has his own medical adviser to whom he refers those who are ill or suspected of illness still leaves the onus of suspecting or "not suspecting" on him.

There is nothing to prevent individual doctors from investigating a heterodoxy but if general medical coöperation is sought for it I still think that it would be wiser to insist on the safeguards which are given say by physiotherapists who do not advertise

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1 Douthwaite, A H Hale White's Materia Medica Pharmacology and Therapeutics London 195*

# Obituary

## HAROLD KIRK WALLER

M B Camb , F R C O G

Dr Harold Waller possessed in full measure the qualities that become a doctor Courteous, gentle, witty, and humble, he had a scholar's wide culture and persistently inquiring mind , and he was a trusted friend to many In particular his perceptive understanding of women was the basis of his special contributions to medicine—his work for the better training of health visitors and midwives and for the education of mothers, and his detailed studies of the processes of breast-feeding He could not have achieved so much without a constancy of purpose amounting to a vocation, yet he never allowed this to obtrude His enthusiasm was tireless, but his persuasion rested on no stronger phrases than a quiet " I think it so important "

[Elliott & Fry

He was born in 1881, the youngest but one in a family of sisters His father, the Rev Horace Waller, had worked in Central Africa with David Livingstone, shared in the anti-slavery movement, and was an intimate friend of General Gordon he died when his son was 15 He was educated at Charterhouse School, Trinity College, Cambridge, and University College Hospital, London On qualifying in 1909 he became house-physician to John Rose Bradford and Batty Shaw Later, while serving as R M O at Queen Charlotte's Hospital, he started with a colleague the first child-welfare clinic In 1911 he was appointed R.M O at the East London Hospital for Children, Shadwell, where he worked under Eustace Smith, J A. Coutts, Morley Fletcher, and also Wilfred Trotter to whose influence he often paid tribute

During his time at Shadwell an epidemic of gastroenteritis overwhelmed the hospital There were more than 3000 cases some cots were even occupied by three dying babies within a day The most up-to-date treatment then consisted in little more than trying to maintain fluids by subcutaneous injections of saline, and a baby's chance of survival depended mostly on successful breast-feeding and on the mother's knowledge of hygiene After that saddening experience, whatever his other activities, Waller's first concern was always the technical details which make breast-feeding possible, and the spread of knowledge about child care

In 1912 he settled in Chelsea, and his large practice was soon chiefly among mothers and children But he also found time to acquire experience of infant welfare under Eric Pritchard who was already urging the need for preventive work among the poorer mothers When, in 1914, the Royal College of St Katharine, in Poplar, became a training-school for the first health visitors and a welfare centre equipped with clinics and a few beds, Waller was appointed superintendent medical officer Except for his war service with an ambulance unit, he remained on the staff until 1948 There he taught the health visitors and with others started antenatal clinics, the first dental clinics for children, facilities for tonsillectomy, and a ward for infants who were not thriving A garden for sunlight treatment and an artificial-sunlight clinic for the treatment of rickets were added in 1921

In 1912 he heard of the work of Mrs Lelia Parnell, Miss Alice Gregory, and Miss Maud Cashmore, who founded the British Hospital for Mothers and Babies at Woolwich Their ideals of better training for midwives and better supervision of the expectant mother appealed to him and he joined them as physician and lecturer to the nurses. Thus began an association which lasted until his death Through it the small unknown hospital in a poor inaccessible district won a reputation throughout the world for the excellence of its care, the training of its midwives, and the original investigat out

For many years his work was thus divided Poplar, Woolwich, and Chelsea where his included many confinements He was a hi obstetrician and has been called the " first of th practitioner obstetricians " In 1927 when Babies' Club was formed he became its me and from his skill and gentle wisdom has com its success But his interest was more and more to child welfare and he gave up his practice in more of his time to research on breast feeding end he received a grant from the Goldsmith's

At Woolwich Waller was able to test his management in breast-feeding He had al to the conclusion that the natural process, if le failed about a third of the babies as a sourc The failure was commonly attributed to the ness of the baby's suction But he questioned we are always right to place on the child th onus of withdrawing the milk " He noticed failure of secretion followed engorgement and prevent it by antenatal expression of viscous postnatal expression to avoid overfilling, the tration of stilbœstrol to reduce tension within and the use of a simple appliance to improve of poorly formed breasts and nipples He importance of the baby's position at the the unending vigilance needed to combat sore nipples He was the first doctor to describe th reflex and to draw attention to its importan difficult, now that his methods have becom established and much of his work is common to appreciate the wealth of patient original observation on which it rested His book, C *in Lactation*, when it was published in 1037, have no word in common with previous to women who had fed their babies from th rang with truth

Most of his work related to breast-feeding, For instance, in the '20s while working at Popl to sit about in dockers' homes to see what had to eat, because dockers were so power He found that their diet included steak, tripe, trotters and he came to recommend a liberal protein diet for weanlings far in advance of th of the time He always kept in touch with background of his patients, and during the b used to visit old people in their shelters and Poplar during the bombing to persuade evacuated During raids on Woolwich he the midwives on their visits to allay fear

He was fortunate in being able to convey his not only in scientific journals and books, b talks, for he was a gifted teacher He had speaking and writing which lightly and easily attention He taught by relating examples memorable because of their humanity The emotions were gripped and yet there was slightest trace of sentimentality an emotional to breast-feeding, so easily assumed, embarr He was among the first to see the possibilities casting as a means of educating mothers in c and he availed himself of it from the early broadcasts were so vivid that many of his listen feeling that he held a real baby in his arms as h

In the past decade his views had won wide He was invited to lecture in America and Ne but ill health prevented his accepting He was able to go to Paris to address an international in 1953 The same year he was elected F.R also received the Dawson Williams prize On ment a fund was raised, primarily by the British Hospital for Mothers and Babies, to tribute to him, bed sitting-rooms for the mothers and babies Though the building complete he saw it begun and took delight in its progress He died at Wadhurst on Jan 1

A G H writes

" I met Harold Waller for the first time at 1911, the year of the great epidemic of gastro-enter the summer and autumn 3118 cases were trea hospital The appalling mortality affected him eve determined him to devote the greater part of onal life to the care of children Time meant little en he was dealing with anxious cases and it was him that he would often awake to the fact that he late at the clinic and that there were appointments m busy in his general practice until midnight or had built an extensive general practice but this tirely satisfy him for his heart was in the problems welfare to which he gave all his energy when he his private work in 1933

the past fifteen years his health was a constant but he never complained and refused to let it is work. His keenness was infectious and he was colleagues and patients His characteristics were kindness, humility and a great capacity for —a handsome gentleman in every sense of the

r old friend F C N describes him as a man gh he held strong views never pushed them

s glad to see others researching along the same nself and never assumed the title of leader although was this to many of us Though he was reserved and eared distant he was not pompous he had an knack of being able to laugh at himself Quite wrote to a friend who had been ill and said Adopt le of the oriental and sit contemplating nothing d this is impossible but in old age it is so seductive en for dignity

## JOHN DUNCAN WHITE

M.B Edin, D.M R.E

ncan White, who retired last year from his ent as radiologist to Hammersmith Hospital r lecturer in radiology at the Postgraduate School of London died on Jan 21 after a s largely due to his work. He was 59 years

duated M.B in the University of Edinburgh d held house-appointments at Edinburgh Royal and the Mansfield and District Hospital On n to civilian practice after service with the he decided to specialise in radiology and he D.M.R.E. in 1921 He was for a time an assistant t at St. George's Hospital London he was l to the staff of St Giles Hospital and of the of St. John and St. Elizabeth in 1924 and of ital for Tropical Diseases in 1927; and in the he also joined the teaching staff of the British of Radiology In 1930 he returned to Edinburgh r of the department of radiology at the Royal ; but after four years there he was chosen to t director of the department of radiodiagnosis ersmith Hospital joining the Postgraduate chool of London as lecturer in radiology He me senior adviser in radiology to the London ouncil a post which he held until the start of nal Health Service in 1948 He continued to Institute of Radiology as a member of its nd in 1935 he was its president. His enthusiasm aching of radiographic techniques had early him into contact with the Society of Radio- and his critical and constructive interest in ty's activities was maintained after his return n.

he was released from his duties at Hammer- spital to take charge of the training of personnel miniature radiography in the Army In 1953 appointed O.B.E. and the following year he

rsonal tribute J F B writes:

h Duncan White taught and showed the highest of radiology to his students radiographers and he did not consider the production of a spectacular his goal but merely a means to help the patient ity enthusiasm, and desire to render to his patients t service radiology could give unfortunately resulted radiation burns which necessitated several amputa hese ominous signs, though associated with much borne silently with great fortitude

R E S writes:

Dr Duncan White was a man of infinite courage—both physical and moral. His encouragement and support can only be appreciated by those who were closely associated with him He was a man of varied interests with a phenomenal memory for detail in connection with his work, a charming host and a most amusing conversationalist—qualities which were greatly appreciated by his many friends. Not only in England but also in the Dominions there are many radiologists holding posts of responsibility who owe a great deal to his foresight and teaching

In his marriage to Mrs. Clare Wigfull eighteen months ago he found great happiness and she proved a constant and devoted companion to him during his long illness

## JAMES BLAKELY MILLER

M.D LL.D Glasg D.P H J.P

Dr J B Miller who died on Jan 14 at the age of 77 was chairman of the Representative Body of the British Medical Association from 1946 to 1948 His years of office were arduous and eventful. They covered the passage through Parliament of the National Health Service Act and the long negotiations between the Ministry of Health and the medical profession before the service was set up The seven meetings of represen tatives over which he presided during these critical times gave full scope to his skill as a chairman

He was born at Kirkintilloch Dunbartonshire the son of the Rev Andrew Miller He was educated at Glasgow High School and Glasgow University where he graduated M B with commendation in 1898 After serving as senior assistant at Town's Hospital Glasgow he settled in general practice at Bishopbriggs a mining and agricul tural town near Glasgow In 1905 he became M D, again with commendation He was also M O.H for the neigh bouring burghs of Kirkintilloch and Kilsyth and in 1909 he took the D.P.H As a citizen, as well as a doctor, he took a full part in the life of the community and his many honorary appointments ranged from justice of the peace for Lanarkshire to the trusteeship of the Cadder and District Miners and Community Welfare Since 1922 he had been actively associated with the work of the B M A. and in 1929 he was elected to the council Since then he has served on many of the Association's committees, notably those concerned with public health industrial medicine and medical planning In 1951 he was elected a vice-president of the Association

When, in 1951, he completed fifty years practice his friends and patients made a public presentation to him. Last year when the B M.A met in Glasgow the honorary degree of LL.D was conferred on him by the university in recognition of his mastery of the difficult [illegible] of general practice

A T R recalls that none of the seven Representative Meetings over which Miller presided was an easy one.

With the National Health Service [illegible] repre sentatives came eager to add the [illegible] of their divisions to the doubts and discontents of the day Miller's experienced chairmanship his sense of the meeting and his patience and never failing humour [illegible] and the Representative Body in good stead. [illegible] giving every speaker his due hearing [illegible] for the moment when debate could give place [illegible] the meetings calmly and [illegible] Representative Body were his friends [illegible] when his chairmanship [illegible] ended and it was a real [illegible] Glasgow meeting last year. [illegible] was as alert and witty as [illegible] pleasure from meeting [illegible] the graduation when [illegible] degree he was aptly [illegible] those virtues which [illegible] revered figure [illegible] revered and loved [illegible] him.

Dr Miller married [illegible] the Rev J B A [illegible] and two [illegible] Miller [illegible]

## CECIL GORDON ROBERTS

B A, M D Camb

Dr C G Roberts, deputy Treasury medical adviser, died on Sept 8, at the age of 48, at Tamworth in Australia while on holiday with his wife

He was educated at Uppingham and at Emmanuel College, Cambridge In 1927 he took the natural sciences tripos, part II, in physiology, a training which later coloured his approach to the problems in industrial medicine He continued his medical studies at the Westminster Hospital. He qualified in 1930 and after holding house-appointments he became resident medical officer at the Westminster Later he was for a time resident physician at Ruthin Castle

In 1934 he joined the medical staff of the General Post Office under Sir Henry Bashford, who was then chief medical officer During the war years his clinical ability, cheerfulness, and optimism did much to maintain the morale of the staff at headquarters, who were then entitled to medical attention under the old Post Office medical service He trained many hundreds in first-aid and he was unstinting in giving of his time to the many charitable and social activities of the Post Office He interpreted the responsibilities of medicine widely, and he had *remarkable success in getting the idea across that* medicine was concerned with every aspect of the well-being of the workers in industry In 1943 he was promoted second medical officer and two years later chief medical officer When the Government medical services were reorganised in 1948 he became deputy Treasury medical adviser His influence during this difficult transitional period was great, and to a large extent the smoothness of this transfer was cooperation

About a year ago he decided to emigrate He was attracted by the scope of industrial there and he wished to give his two sons in a new country During his last few Treasury he initiated many changes, and he by many doctors on industrial medical of them, J N M., writes

"When the Social Medicine Research Unit years ago to set up epidemiological studies on disease, Roberts was one of the first to whom advice and help He was immediately *and thereafter, until he left for Australia*, we the experience of postmen and other grades organisation he served He was a delightful with—warm, enthusiastic, and full of ideas. unusual breadth of interest, and a rich fund of the people for whom he was caring At the was actively concerned with mass statistics and of large scale administration His physiological him insight into the "human engineering" job, his psychological interests led to useful both theoretical and practical, on health and relation to the size of working groups He *great clarity on topical questions of industrial* political developments that came from the Service and the growing concern of trade unions matters, and, particularly, about current human side of industry, in welfare, personnel the human relations' movement At a time medicine is having difficulty in finding its order of things his counsel will be sorely missed"

## Diary of the Week

JAN 30 TO FEB 5

### Tuesday, 1st

British Postgraduate Medical Federation
5 30 P M (London School of Hygiene and Tropical Medicine, Keppel Street W C 1) Dr E F Gale Actions of Antibiotics on Bacteria

St Mary's Hospital Medical School, Paddington W 2
5 P.M Mr Aleck Bourne Functional Uterine Hæmorrhage

### Wednesday, 2nd

Institute of Laryngology and Otology, 330, Gray's Inn Road, W C 1
6 P M. Prof M. Arslan (Padua) Effects of Ultrasonic Waves on the Ear

Institute of Dermatology, St John's Hospital Lisle Street, W C 2
5 30 P.M Dr J O Oliver Bacteriology of Skin Diseases

Institute of Diseases of the Chest, Brompton S W 3
5 P M Dr J G Scadding Investigation of Respiratory Illness

Birmingham Medical Institute 154 Great Charles Street Birmingham 3
8 15 P M Mr A Ruscoe Clarke Blood loss and Blood transfusion in Civilian Trauma

Manchester Medical Society
4 30 P.M (Medical School) Prof John Glaister Some Medicolegal Trifles

Medico Chirurgical Society of Edinburgh
8 30 P M (Royal College of Surgeons 18 Nicolson Street, Edinburgh.) Dr G A Grant Peterkin Place of Dermatology in Medicine

### Thursday, 3rd

Royal College of Surgeons of England, Lincoln's Inn Fields, W C 2
5 30 P M Sir Gordon Gordon Taylor Swellings of the Neck and their Management

Royal Army Medical College, Millbank, S W 1
5 P M Prof Charles Rob Preservation and Transplantation of Human Blood vessels

British Postgraduate Medical Federation
5 30 P.M. (London School of Hygiene and Tropical Medicine) Prof P B Medawar, F R.S Tissue Transplantation Immunity

Institute of Psychiatry Maudsley Hospital Denmark Hill S E 5
5 P.M Prof H J Eysenck Psychology and the Foundations of Psychiatry

Nuffield Orthopædic Centre, Wingfield Morris Orthopædic Hospital Oxford
8 30 P M Dr E G L Bywaters Natural History of Rheumatoid Arthritis

Liverpool Medical Institution 114 Mount Pleasant Liverpool, 3
8 P.M. Dr V K Summers Syndrome of Hypothyroidism

University of St Andrews Medical School, Small's Wynd Dundee
Dr T Anderson Unwanted Effects of Chemotherapy

### Friday, 4th

University of London
6 30 P M (London School of Hygiene and Trop Dr J A Scott Health

Postgraduate Medical School of London Du
4 P M Prof R E Tunbridge Disorders of Con

Royal Society of Medicine 1 Wimpole Street W
10 30 A M *Otology* Mr J W S Lindahl Dr R Malignant Disease of the Middle Ear and M
2 30 P M *Laryngology* Dr W Brockbank, Dr Mr J C Hogg Relation of Nasal Disease
5 30 P M *Anæsthetics* Dr J E Hall Respiratory Infants and Young Children

Institute of Dermatology
5 30 P M Dr P J Hare Clinical demonstration

Royal Faculty of Physicians and Surgeons 242, St Vincent Street, Glasgow
5 P M Mr J Sloan M Robertson Paralysis Problem

## Appointments

Davies R G M D Lond D.P.H deputy M.O.H. and principal school M O Kingston upon Hull and and medical inspector of aliens, Hull and Goo authority

Deegan, John M.B Durh school M O, Northumb

Gowans J A L.R C P.E senior casualty officer

Hendrie Margaret I M D Lond, D.P H D C.H. M O (maternity and child welfare) Kingston up

Kelsall, P D, M B Manc F F A R.C.S, D.A con thetist Southport, Ormskirk and North Liverpool

Lederer Josef M R.C S, D A consultant an West Durham H.M C

Lockhart Mummery H E M.A M CHIR. Camb., F.R. surgeon (consultant status) Italian Hospital Lo

Matthews, R A M.B Lond school M O Norther

Moynagh D W, M B Lond D.P.M whole time psychiatrist, Mapperley Hospital, Nottingham

O Reilly John D M. Oxfd M R C P honorary ician children's department, Hospital of St Elizabeth London

Roads P G M D Lond, D P H deputy M O H., St

**East Anglian Regional Hospital Board**

Foster Smith G C, M R.C.S D A asst anæ and Norwich hospital group

Tagart R F B M CH Oxfd F R.C.S cons Newmarket General Hospital

Thompson J R. M CHIR Camb F R.C.S cons Peterborough and Stamford hospital group

**Appointed Factory Doctors**

Ballance G A M.B Camb Knighton Radn

Shearer J A. W M B Edin Newtown, Montg

Williams R D M B Camb Stevenage, Hertf

# Notes and News

## WORLD HEALTH ORGANISATION

eenth session of the Executive Board of W H O Geneva on Jan. 18 under the chairmanship of van Zile Hyde (U.S.A.) It was announced that t few months the Organisation had set up a net poliomyelitis research laboratories which would extended These laboratories would study and ocal strains of the viruses of poliomyelitis and of eases—in particular those of encephalomyelitis rd adopted a resolution to give first priority in the ublic health to the promotion of research into the radioactivity Dr M G Candau director general said that early planning was needed if the dangers n the increasing application of atomic energy to were to be avoided The W.H O programme was to include the collection and dissemination of on on the medical and biological aspects of atomic d the training of personnel in methods of protection

## SCHEME FOR JUNIOR HOSPITAL STAFF

xford Regional Hospital Board is introducing into s hospitals a scheme designed to meet the needs of ctors who on completion of their National Service extend their experience before entering general r being selected for training as specialists. Many young doctors are married and find themselves r financial and other reasons to take up short ts in the hospital service

eme provides for the creation of a limited number of intern posts in the salary grade of junior hospital fficer (£775 × £50 to £1075) to take the place of osts on the junior hospital staff They will be tenable ars and will be held in the Reading and Northampton f hospitals (four posts in each group) Every effort ade to provide accommodation for married doctors r the hospitals at an economical charge

s of these posts will be expected to serve for approxi months in each of the major departments of the medicine surgery pædiatrics and obstetrics) and to the other departments as circumstances in the day nning of the hospitals may require

ought likely that most of those holding these posts more years will elect to enter general practice and nority will wish to train as specialists in branches of to which they are specially attracted or for which e a special aptitude The latter (if selected by their t) will have the opportunity to take up posts in the departments of their own or other hospitals in the taining the salary increments in their grade

egional committee of the executive councils has l its interest in this project and willingness to in facilitating the entry into general practice of rained under the scheme

## LOIASIS

eeting of the Royal Society of Tropical Medicine and in London on Jan 20 members of the staff of the l School of Tropical Medicine and their colleagues under the Colonial Medical Research Committee l researches on loiasis in the British Cameroons.

R. M Gordon showed that various species of chrysops en confirmed as actual or potential vectors that l infected from man can transmit the infection to monkeys that the *infection is widespread in the* on of many rural areas of West Africa though the l incidence is often less than would be expected from of the biting habits and the infection rates of the and that as yet we do not know enough of the history of this disease and particularly of the extent ortance of monkey reservoirs, to institute large and e schemes of control

ast point is implicit in the study of chrysops species tribution and breeding reported by Mr W Crewe H Oldroyd *C silacea* is the vector par excellence umba area because its behaviour allows the requisite with man Chrysops seems to be a genus of savannah d from which a few species have migrated to the ing Dr B O L Duke has observed that *C silacea* cted to wood smoke; it bites through most of the hours and therefore has a maximal chance of picking up the microfilariæ of *Loa loa* which shows the well known diurnal periodicity of this species But loiasis in mandrills infected with adult *L loa* taken from a naturally infected mandrill showed nocturnal periodicity; so far no essential difference has been found between human and monkey strains.

Prof J J C Buckley discussed the general features of development and ecdysis of microfilariæ in insect hosts and Dr Frank Hawking filarial periodicity He has in previous work shown that periodic microfilariæ seek the capillaries of the lungs at certain hours of the day this probably being the optimum site for them.

Dr W E Kershaw has studied the epidemiology of this infection in the rain forest its abrupt fringe the mountain grassland and coastal areas taking into consideration the population and its distribution in urban and plantation areas His empirical approach to these problems was supplemented by an analytical approach of great interest in which a mathematical model was constructed on the basis of the factors involved

In the discussion Sir George McRobert referred to the psychological effect of this infection in European residents of the endemic area and to the fact that the pathological effects of these migratory adult worms are little understood Prof A W Woodruff spoke of the importance of exact diagnosis since the value of diethylcarbamazine can be seriously underrated if wrongly given in non specific allergic states. Apart from the finding of microfilariæ (in which recent concentration techniques are valuable) eosinophilia, the complement fixation test and a recent history of Calabar swellings are important pointers. Diethylcarbamazine can eradicate even long standing infections.

## RESEARCH IN CEREBRAL PALSY

The Nuffield Foundation is financing a five year programme of research at Frenchay Hospital Bristol into the neuropathology of cerebral palsy and mental defect This grant will enlarge the scope of the work already being carried out by the Burden Mental Research Department of the South Western Regional Hospital Board The Burden Research Committee under the chairmanship of Dr J G Greenfield has been responsible for long term investigations into mental deficiency and the neuropathological side of these researches has been under the direction of Dr R M Norman, lecturer in neuropathology at the University of Bristol who has recently been given a full time research appointment by the board

A new laboratory is now being equipped and Dr H Urich, a lecturer in the department of pathology of the university has been appointed to assist Dr Norman The work will be undertaken in coöperation with the departments of pathology and child health of the university Its main purpose is to examine the brains of patients who have suffered from cerebral palsy and whose early history and clinical condition have been adequately recorded There are at present few detailed studies of both clinical and pathological data and for this reason much uncertainty exists as to the part played by birth injury in the pathogenesis of cerebral palsy

The new research team will have access as in the past to cases from the local hospitals but it is hoped that when the new laboratory is in operation clinicians and pathologists from other regions who have suitable material will use the facilities at Frenchay for the detailed examination of the nervous system.

## BACTERIA IN INDUSTRY

Even among culture collections there is increasing specialisation and several new ones were created in 1950 on the decentralisation of the Medical Research Council's National Collection of Type Cultures One of these the National Collection of Industrial Bacteria has just published a catalogue[1] of bacteria primarily of interest to industrialists but this catalogue also contains two lists of wider interest The first is a list of compounds produced by different micro organisms maintained in the Collection—e.g., acetone is produced by three strains of *Clostridium acetobutylicum* and penicillinase by two strains of *Bacillus licheniformis* and by one of *B subtilis* The second is a list of strains used for microbiological assays; folic acid can be assayed either by *Lactobacillus casei* NCIB 6010 or by *Streptococcus fæcalis* NCIB 8123

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[1] The National Collection of Industrial Bacteria Catalogue of Strains HM Stationery Office Pp 34 2s

## THE ELDERLY WORKER

In his third report[1] on the later working life in the building industry (part of the Nuffield Foundation's inquiry into the needs of old people), Mr F Le Gros Clark assesses the extent to which special use is made of older employees Most firms which he questioned agreed that older workers should relinquish constructional work for less arduous duties of maintenance and repair Few favoured grouping elderly employees in separate gangs, since young workers learn much from their older colleagues, who in turn obtain considerable assistance from their stronger and more agile juniors Mr Le Gros Clark concludes that the building industry will be able to employ an increasing proportion of elderly craftsmen, provided always that careful attention is paid to finding them work of a suitable nature

### University of London

Dr Otto Klineberg, of the Department of Social Sciences, UNESCO, and professor of psychology at Columbia University, is to deliver two lectures, on Feb 14 and 15 The first is entitled Psychology and International Relations, and the second Uses and Limitations of the Experimental Method in Social Psychology Both lectures will be given at 5 30 P M, at the Senate House, W C 1

### University of Birmingham

Dr W Mayer Gross, part-time consultant psychiatrist at Uffculme Hospital, has been appointed senior fellow in the department of experimental psychiatry Dr Mayer Gross was formerly director of clinical research and consultant psychiatrist at Crichton Royal Mental Hospital, Dumfries Dr K H Ginzel has been appointed senior research fellow in neuropharmacology, and Dr P B Bradley lecturer in electrophysiology, in the department Dr J Williams has been appointed lecturer in anatomy

### Royal College of Physicians of London

On Tuesday and Thursday, Feb 8 and 10, Dr J A Smiley will deliver the Milroy lectures, on Personal Factors in Accident Proneness Both lectures will be given at the College, Pall Mall East, S W 1, at 5 P M

### Society of Apothecaries of London

At recent examinations the following were successful

*M M.S A* —A P Camilleri, S Miller
*L M S S.A* —R N Wade, P M Gurring, P Jago F R. F Dibb T Freuchen, A P Brown, E A Capell, D A Bennett, J E Todd J A. Bradford
*D.I H*—Z Khan, W H Suffield

### North of England Obstetrical and Gynæcological Society

The following officers have been elected for this society for 1955

President, Mr H J Malkin hon treasurer Mr C H Walsh hon general secretary Mr J B Cochrane, hon reporting secretary Miss U M Lister

### British Association of Plastic Surgeons

The following officers and council have been elected for 1955

President Prof T Pomfret Kilner, hon treasurer, Mr R. P Osborne, hon secretary, Mr J P Reidy council, Mr J N Barron Mr W Hynes Mr P H Jayes, Mr D N Matthews, Mr Rainsford Mowlem Mr Mortimer Shaw, Mr J S Tough, Mr A B Wallace

### College of General Practitioners in Scotland

The Scottish council of the college was constituted at a meeting held in Edinburgh on Jan 13 Dr J M Henderson (Pitlochry) was appointed chairman, Dr Lowell Lamont (Edinburgh), vice chairman, and Dr Richard Scott (Edinburgh) hon secretary and treasurer Other members of the Council are

D Peebles Brown (Kilmalcolm) Mary Esslemont (Aberdeen) C M Fleming (Edinburgh) W W Fulton (Glasgow) W S Gardner (Glasgow) I D Grant (Glasgow) G W Ireland (Pathhead) K A Mackay (Laggan) T S McDonald (Glasgow), J G Munro (Beauly) David Myles (Forfar) R A. B Rorie (Dundee) C S Sandeman (Durness), J A Shearer (Bucksburn) J M Stalker (Dundee) and George Swapp (Aberdeen)

The Scottish office of the College is at Livingstone House, 39, Cowgate, Edinburgh, 1

### Course on Child and Family Psychiatry

The department of child psychiatry of Ipsw group is holding a refresher course on this March 28 to April 1 Further particulars may b the Child Psychiatry Clinic, 11, Fore Street, Ipsw

### International Symposium on Cardi

A symposium on Cardiovascular Surgery in Physiology, Diagnosis, and Techniques is to b Detroit on March 17–19 Inquiries should be the secretary of the symposium, Henry Ford Hosp 2, Michigan, U S A

### Royal Institute of Public Administration

This institute is to hold a conference, under the ship of Dr May Baird, at Peebles from March 31 on the National Health Service The theme of ference is to be Working Together—Progress and The opening speaker will be Sir Humphrey chairman of the South Eastern Regional H other speakers will include Dr J O McDonagh, the Scottish Association of Executive Councils, Jardine, chairman of the General Board of Dr M M Whittet, physician superintendent of Hospital, Inverness Further particulars may b the hon secretary of the Edinburgh and East of regional group of the institute, 245, High Street,

### Lady Tata Trust

The trustees of this fund invite applications scholarships, or fellowships for research on blood, with special reference to leukæmia In affinity between leukæmia and other forms of disease, candidates who wish to undertake aspect of malignant disease which may throw light on problems of leukæmia will be eligible

Grants are made for research expenses or to provi or technical assistants for senior workers Scholarships of £600 per annum) are awarded for the personal of workers carrying out approved research under su In addition the trustees may award one or more fellow p a ) to workers with considerable research experien particulars may be had from the secretary of the sci committee c/o Medical Research Council, 38 Old Q London, S W 1 Applications must be submitted before

### Dinner to Dr W E Lloyd

On Jan 15 Dr Lloyd's former house physic Westminster Hospital and the Brompton Hospital Chief a dinner Despite bad weather 45 gathered from all over the country The occasion was by any special anniversary, but by the hosts wish their "affectionate regard for the most wise and physicians" Dr Lloyd included in his list of ideal a houseman—loyalty, enthusiasm, and a calm understanding of human nature (including the All these found expression in speeches extolling the figure known throughout his hospitals as 'Erne

*NP 13* —Messrs Nicholas Products Laboratories Bucks, inform us that the NP 13 ('Megimide Dr Harris (Jan 22, p 181) and other workers was Nicholas Proprietary Ltd , Melbourne Within a Nicholas Products Laboratories hope to have supplies of this drug for clinical trial

*Guida Villit* —This 800 page illustrated guide to Ita resorts includes a list of spas and the medical conditi they are recommended. It is issued by Ufficio Sta Italiana, Via Budua 13, Milan

CORRIGENDA *A Barbiturate Antagonist* —In the week by Dr T A B Harris (p 181) the reference to a Shaw and his colleagues (1954) should have read 174, 402

*Gloucestershire County Council* —The council i invit tions for the appointment of deputy county medical of and deputy principal *school* medical officer In the issues the word 'school' was omitted The correctly in this issue

# Births, Marriages, and Deaths

## BIRTHS

LEVINSON —On Jan 21, at the London Clinic Levinson (née Dove), wife of Ellis Levinson—a
TAYLOR —On Jan 15 at Godalming, to Phyllis (née wife of Dr W K Taylor—a son
WRIGHT —On Jan 19 at 64 Redbrink Crescent Sheila (née Smith) wife of Dr Martin Wright—a

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[1] Aging Men in the Labour Force The Problems of Organising Older Workers in the Building Industry By F LE GROS CLARK M.A Obtainable from the Nuffield Foundation Nuffield Lodge Regent's Park London N W 1 1955 Pp 18

# THE HUMAN SOURCE OF
# CULOUS INFECTION IN CHILDREN

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ommon knowledge that tuberculosis in children ventable disease yet by the time children in reach their fourteenth year some 45% of them n infected with tuberculosis (Medical Research 1952) The mortality from tuberculosis in child fallen rapidly in the last few years largely as of improved methods of treatment, but the *fall* culosis morbidity has not kept pace with the ortality (Lorber 1953) For this reason we have detailed investigation of the source of infection e group of tuberculous children This was on lues to a smaller investigation of 150 children erculous meningitis or miliary tuberculosis which ented by one of us to the British Pædiatric on (Lorber 1950)

the present investigation we were repeatedly d by the frequent occurrence of certain prevent les of infection in children and it is these which put together for the purpose of this paper

### Material and Method of Study

otal of 564 children with active intrathoracic or ed tuberculosis there were 367 (65 2%) in e source of infection was determined A really search for the source of infection was made in ese 564 children—the search including the whole d together with persons who on the basis of ry appeared to be likely sources of infection n source of infection was finally discovered in these 401 children (81 5%) (see table) The were either inpatients in the Children's Hospital eld between Jan 1 1947 and Dec 31 1952, or nts attending the tuberculosis contact clinic in dren's Hospital between 1940 and 1952 inclusive e 401 patients were admitted because of miliary geal tuberculosis. 73 of the 401 children (18 2%) der one year of age and 101 (25 1%) were one and two years of age Information regarding ce of infection was collected up to and including 1954 For the purpose of this study entire histories were sometimes re-assessed and the re-examined with the help of chest physicians

evidence that a child has been infected by a uberculous person can never be absolute When d however that an infected child had been in ed contact with a person suffering from active ary tuberculosis or with a person with an potentially discharging tuberculous lesion we that person as the source of infection. Some ore than one such person was in contact with In other cases the chest physician reported that in contact with a child had recently had an ous which was now quiescent If no other definite was discovered then such persons were accepted as probable sources of infection Hearsay evidence of contact with tuberculosis or of contact with a person with a chronic chest infection of doubtful ætiology was not accepted as evidence of contact with tuberculosis, nor were other children suffering from uncomplicated primary tuberculosis accepted as sources of infection

### Summary of Results

The source of infection was determined in 327 of the 401 children (81 5%) who were adequately investigated. It is known that in some of the children in whom no contact was found the infection was of bovine origin

As one would expect the younger the child the easier it was to trace the source of infection In the adequately investigated families the source of infection was found in 70 (95 9%) of 73 children under one year of age in 86 1% of the 101 children aged one year in 84 6% of 117 children aged two to four : and in 64 5% of 110 children aged five to fourteen In some cases there were multiple contacts The father had tuberculosis in 119 instances the mother in 108 other relations in 143 and other persons in 46 It is apparent that most of the sources of infection were within the household for over three quarters of the contacts were parents or other persons living in the house

### Observations on the Results

From our knowledge of the source of infection in the above children we have brought together some of the more important means at our disposal for preventing tuberculous infection in children We have arranged these under headings illustrating most of the headings by one or two stories to show the consequences of lack of attention to detail in the measures indicated All these stories could be repeated many times We do wish to emphasise that these stories are not given in any spirit of criticism their sole purpose is to emphasise the importance of the measures described in the prevention of tuberculosis They represent failures, and in giving them we are not at all unmindful of the tremendously valuable work of the tuberculosis services in the prevention of infection The following are the measures which we wish to emphasise

THE SOURCE OF INFECTION OF 564 CHILDREN WITH INTRATHORACIC OR GENERALISED TUBERCULOSIS
(Adequately and inadequately investigated families)

| — | Contact found | | | No contact found |
|---|---|---|---|---|
| | Known beforehand | Discovered afterwards | Total | |
| Adequately investigated families (401) | [illegible]1<br>*(7[illegible]%)* | 16<br>*(11 4%)* | 327<br>*(81 5%)* | 74<br>*(18 5%)* |
| Inadequately investigated families (163) | 37<br>*([illegible]7%)* | 3<br>*(1 8%)* | 40<br>*(24 5%)* | 123<br>*(75 4%)* |
| All families (564) | 318<br>*(56 3%)* | 19<br>*(3 7%)* | 367<br>*(65 )* | 197<br>*(35%)* |

(1) *The avoidance of delay in radiological examination in the presence of symptoms suggestive of tuberculosis*

Though active tuberculosis in an adult can be asymptomatic, in our experience symptoms were usually present but their significance was not realised and there was serious delay in arranging radiological examination For example a man was treated at home for pneumonia for six months, and apparently no doubt was felt about the diagnosis It was only when his two year old boy was admitted to hospital with tuberculous meningitis that he was X rayed and found to have tuberculosis. A mother of two young children had had a cough for five years and had been treated for chronic

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nt of a grant from the Tuberculosis Research Fund of the rsity of Sheffield bronchitis She was unduly tired during pregnancy, and it was some months after delivery before she was X-rayed on her own initiative by a mass-radiography unit, and found to have tuberculosis By that time both her children had been infected

(2) *Determined and persistent efforts to persuade a suspected contact to have a radiological examination*

One by one all 14 children of a family contracted tuberculosis and 2 of them died The father had a chronic cough, but he refused an X ray examination on the grounds that he was "too nervous" to have that done No-one other than a health visitor had attempted to persuade him

(3) *Notification*

Many tuberculous persons—children and adults—are not notified Cases of tuberculous cervical adenitis, or of tuberculosis of the kidney, bones, or joints are particularly liable to be left unnotified Quite often a case is not notified because of the erroneous belief that someone else has done it Sometimes notification is avoided because it is felt that such a step might expose the patient to a social stigma or handicap him in other ways, such as obtaining jobs, or in obtaining life-assurance policies after recovery In other cases evidence of activity of the tuberculous process is in doubt A positive tuberculin reaction as the sole evidence of tuberculous disease is not acceptable to the authorities as a reason for notification, although it is obvious that the notification of young children with a positive tuberculin reaction may well lead to the discovery of an open case of tuberculosis Sometimes notification is missed simply by default There would seem to be good grounds for establishing a modified form of notification, which would not expose the patient to any possible disadvantages, and yet would allow the chest physician to examine for the source of infection and protect other contacts

(4) *Continued supervision of adults who are thought to have inactive tuberculosis*

A diabetic was examined at a chest clinic when his five year old, daughter was notified as a case of primary tuberculosis He was found to have an "inactive apical nodular fibrosis" and was discharged from the clinic Subsequently he developed backache and had hæmoptyses, but he was not re examined until another child, who had not been born when the man was first seen, developed tuberculous meningitis Another four month-old baby in this family also became infected and developed meningitis The father was now found to have advanced tuberculosis, and he died in spite of treatment

There is often delay in the diagnosis of tuberculosis in diabetic patients The special liability of diabetic subjects to develop tuberculosis is not always remembered, so that routine X-ray examination is not done

(5) *The treatment of "sputum negative" adult sufferers as potentially infectious if they are in contact with children*

We frequently found that children had become infected with tuberculosis because it was assumed that the adults with whom they were in contact were non-infective because the sputum was "negative" In some cases only a single specimen had been examined As a result of reliance on this laboratory finding, the children were not given protection by B C G Many of the patients, furthermore, were under the impression that they had not got tuberculosis at all

A non tuberculous child had a chronic medical ailment necessitating visits to hospital twice weekly for several months His mother complained that she and her child had every week to share an ambulance with adult patients who were being taken to a sanatorium for refills for their artificial pneumothorax This statement was confirmed by the local authority, who assured us the patients were "sputum negative"

(6) *Determined efforts to avoid the tuberculosis by children from neighbouring the homes of infected adults to watch television with their children, or for other purposes*

We know of several instances of families of ill patients acquiring a television set for th ment Unfortunately the children in the learn about it and gather round the set As a of this, we quote a letter from a chest physi to our inquiry about the contacts of a boy culous meningitis

> " the mother and father in this case have and are normal There seems little doubt that probably became infected at a neighbour's ho frequently went in to see the television and m we have a positive case of tuberculosis As a matte we have another boy of thirteen with a pleural also went and enjoyed this television "

(7) *The prevention of tuberculin negative ch acquiring tuberculosis while attending chest cli clinics, or hospital outpatient departments*

Children may contract tuberculosis while chest clinics and hospitals for contact other reasons In many such clinics there are for keeping uninfected children away from attending such clinics Furthermore, adults tuberculosis often have to take their children tion, because there is no one else to take them we know of several examples of infection by t but it is impossible to prove such infections

An example of this was brought to light wh was referred to one of us from an infant we because of a behaviour disorder It transpir mother had chronic pulmonary tuberculosis a in sanatoria on more than ten occasions. He was taken away from her for three months a nursery until B C G vaccination had been After that she regularly attended an ordina clinic with her baby and freely mixed with oth and babies who had not had the benefit of B C tion and who were unaware of the danger to were exposed The attention of the medica health was drawn to this case He matter further and found that 34 mothers attended with their infants the ordin clinics in his area and freely mixed with oth This practice has now been discontinued

We are fully aware of the difficulty of uninfected children from coming into co infected adults in chest clinics, but it can nea be done with proper arrangements and fores

(8) *Full and adequate instructions of infect elementary hygiene*

When tuberculous adults had to wait for to a sanatorium, or were discharged from a after treatment, we often found that they had no instructions in elementary hygiene as re sputum and did not realise that they wer from an infectious disease A young woman monary tuberculosis and tuberculous laryn offered to look after a young baby while t went out to work, not knowing that she was harm The child contracted miliary tubercul

The responsibility for health education is of the chest physician, partly that of the fa and partly that of the health visitor It is a opinion whether there should be special t health visitors or not, but it would seem that place for more intensive training of health vi important aspect of tuberculosis prevention

(9) *Instruction of parents in the importance of their children from coming into contact with kno from the disease*

adfather was admitted to a sanatorium with sis While an inpatient there he repeatedly is daughter's home (which was not his own nd as a result he infected his seven year old ld who developed miliary tuberculosis

*he avoidance of unnecessary contact of an infected h children*

ten found that tuberculin negative infants and were allowed to visit relations in tuberculous hospitals and sanatoria This could certainly be Patients under treatment were allowed to go weekends and holidays using public transport ct their children or the children of friends or who had not been protected by B C G

*rotection of tuberculin negative children by B C G are known to be about to be exposed to tuberculosis further contact cannot be prevented*

were discharged from sanatorium after treat thout steps being taken to prevent contact with or without protecting the children by B C G only when an adult was found to have tuber no *immediate* effort was made to determine children in the family were still tuberculin in order that they could be immediately from further contact and given B C G Instead continued contact was allowed even nursing being allowed to continue to breast-feed their

*dequate segregation of children from contact ng given B C G*

und that some children were undergoing B C G ion without segregation from an infectious adult *tion is irksome and occasionally difficult to* but it is almost always possible Failure to e a child from contact for six weeks before sion and until tuberculin conversion after vaccina oses the child to infection and gives the parents a se of security It is a practice which brings accination into disrepute

## Discussion

ave made no attempt to give a comprehensive of all the various measures which are important revention of tuberculosis in children We have not d for instance the provision of safe milk We owever picked out from our experience certain s which we think need re-emphasising in that ften see tragedies because these measures have n applied, or because there was *delay in their* ion We are convinced that a greater sense of is needed When a child is notified as having l tuberculosis *every possible effort should be made tely to determine the source of infection, however* That this is very well worth while is convin emonstrated by our figures The source of infection monstrated in 81% of 401 children who were ately' investigated—*thus making it possible* the infected adult to prevent further dissemina infection among children and others and to immediate contacts by B C G if they had not been infected

act that the source of infection could be found in f the children under one year of age is of particular nce. It is of equal importance that in the older p—namely in children five to fourteen years old rce could be found in 64 5% of the cases The nce of this latter fact lies in the attitude so often that in the case of the older child the possible of infection are so numerous that it is hardly while making the effort to look for them Our belie that idea We think it extremely likely, nore that with still more vigorous efforts our for the frequency with which the source of infection was found could be quite considerably improved We think that the figures would be improved by examining other contacts, when examination of the immediate family has proved negative

Just as it is essential when an infection in a child is notified, to look immediately for adult contacts so it is essential, when an adult is found to be infected with tuberculosis to conduct an *immediate* examination of all child contacts, so that further contact can be prevented if the child is still tuberculin negative and he can be protected by B C G if subsequent contact is unavoidable A real sense of urgency is vitally necessary if further tuberculosis is to be prevented

We have re-emphasised the importance of instructing infected patients in the elements of hygiene with regard to their sputum and in particular with regard to their infectivity All too often one sees tragedies in the way of serious infections in childhood which have arisen simply because an adult with tuberculosis was unaware that he was infective particularly to children

The value of the work of the tuberculosis services is reflected by the remarkable fall of childhood tuberculosis mortality in Sheffield (Lorber 1953) It was shown that the mortality in childhood from tuberculosis was lower in Sheffield in 1951 and 1952 than in any other city (The mortality in 1953 remained the same as in 1952 —namely 1 8 per 100,000) We draw cases however from a very wide area, and there is still a great deal of morbidity due to tuberculosis in Sheffield and in the surrounding region Much of it can be prevented by further vigorous and determined efforts.

## Summary

A search was made to determine the source of infection in 564 tuberculous children suffering from intrathoracic, miliary or meningeal tuberculosis The source of infection was determined in 307 children (65 2%) but what was considered to be an adequate search for a contact was made in only 401 cases

In the 401 adequately investigated cases the source of infection was found in 327 children (81 5%) It was found in 95 9% of 73 children under one year of age, in 86 1% of 101 children aged one in 84 0% of 117 children aged two to four and in 64 5% of the 110 children aged five to fourteen

It is very important to notify all cases of childhood tuberculosis so that an intensive search for the source of infection can be made This enables the infected adult to be treated and other child contacts to be protected from infection by B C G or other means It is also important to examine all child contacts immediately when an adult is found to have tuberculosis so that tuberculin negative children can be segregated until they have been protected by B C G We feel strongly that a greater sense of urgency is required in these preventive measures

Other anti tuberculosis measures which require far more attention are

(1) Chest X ray examination of all adults with symptoms that might be due to tuberculosis.

(2) Chest X ray examination of all adults who may be a source of infection

(3) Continued supervision of adults whose tuberculosis is supposed to be inactive Former patients who are "sputum negative' should be regarded as potentially infectious if they are in contact with children.

(4) Prevention of contact between unprotected children [illegible] adults with tuberculosis. Tuberculin negative children [illegible] be *excluded from tuberculous wards of hospitals an* [illegible] at visiting time

(5) Instruction of adult patients in the infective [illegible] condition and in elementary hygiene

We have also mentioned the value of [illegible] who cannot permanently be prevented [illegible] contact with infected adults

We wish to thank all the numerous chest physicians from a wide area who have taken part in the search for contacts of affected children We are particularly indebted to Dr H Midgley Turner, chest physician at Sheffield, for his great help and for reading and criticising this paper without his aid the investigation would have been impossible To Dr Llewellyn Roberts, medical officer of health for Sheffield, we are grateful for reading this paper, and for his coöperation Prof Alan Moncrieff kindly read and criticised the paper We also thank all the health visitors who have done so much essential work in the search for contacts

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## THE SPECIAL SIGNIFICANCE OF CONCOMITANT GASTRIC AND DUODENAL ULCERS *

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THOUGH duodenal and gastric ulcers have much in common, causing similar symptoms and having similar histological appearances, there are quite striking differences between the sorts of people who are attacked by the two lesions Not only are there well known variations in age, sex, and racial distribution, but also the patterns of gastric secretion and muscle tone exhibited by duodenal and gastric ulcer patients lie at opposite ends of the scale , for, whereas duodenal ulcer develops on a basis of hypersecretion of acid, hypertonicity, and rapidity of gastric evacuation, gastric ulcer is associated with a rate of acid secretion below (on the average) that of normal subjects, and with stomachs which are sagging, sluggish, and slow in emptying

That duodenal and gastric ulcers may nevertheless be sometimes found together has been held by some to be evidence of common ætiological factors, for concomitance is twice as frequent as it should be on chance alone Indeed, if they have similar origins, gastric and duodenal ulcers might be expected to occur together not infrequently in persons whose anatomical and functional characteristics lay midway between those associated with each ulcer alone But these are not the sort of people who get such dual lesions

My own opinion, however, is that, whereas the main cause of duodenal ulcer is disproportion between the amounts of acid and alkali reaching the duodenal bulb, the main cause of gastric ulcer is gastric hyposecretion, with its attendant hypomotility On this basis one would expect ulcers of the two organs to be mutually exclusive, and in cases of concomitance some special factor would have to be at work The present investigation was undertaken to discover what this factor might be

### Incidence of Concomitant Ulcers

Though single instances had been recorded previously (Mix 1913, Bonchut and Durand 1913), Sir David Wilkie (1926) seems to have been the first to draw attention to the comparatively frequent coexistence of ulcers in stomach and duodenum He reported that in a series of 300 of his own patients he had found combined ulcers in 42, 16% of those with duodenal ulcers also having gastric ulcers and no less than 53% of the 79 gastric ulcers being associated with duodenal ones The burden of Wilkie's paper was his suggestion that undiagnosed concomitant gastric ulcer might be a reason why gastro enterostomy did not always relieve symptoms attributed ulcer

Little attention was paid to Wilkie's figu though they were , indeed even to the pre coexistence of gastric and duodenal ulcers se struck no-one as remarkable, and scant refer to be found in the most recent and comprehe on peptic ulcer

Hurst and Stewart (1929) described chronic ulcers or scars in both organs as infrequent " and referred to 4000 post morte tions at which 173 chronic gastric and duodenal ulcers were found, but of wh revealed associated ulcers (5 5%) They these figures were difficult to reconcile wi Wilkie

There is no doubt, however, that Wilkie l alone and that the experience of many other continued to be different from that of ph radiologists as well as that of pathologists because concomitant ulçers are more nume patients whose symptoms are severe and and who are therefore referred for operatio

Some 10–15% of peptic ulcers, it is said, ar able radiologically, and I have myself opera patients with peptic ulcers which had not on repeated X-ray examination—including a gastric and a duodenal ulcer The effect proportion of ulcers at radiography is to apparent frequency of concomitant ulcers. if 15 ulcers were missed among 100 patients, had both kinds of ulcer, the apparent rate of would be reduced from 10 to 8%

Though physicians tend to see the earlier surgeons the late ones, the greater frequency tant ulcers in surgical practice cannot at f explained by the longer duration of the illn proportion of ulcer cases with a double le at necropsy Nowadays perhaps most pati condition lose their stomachs before they re mortem room, but this was certainly not so Hurst and Stewart reported The discrepan arises through the discovery, after death, of (as well as some larger) solitary ulcers who was not suspected during life , and the ulcers (most of which will already have clinically) form a smaller proportion of the bigger total The figure for concomitance pathologists before the period of widespread is likely to be the truest one for the living a the dead

TABLE I—AGE AND SEX DISTRIBUTIO

| Age groups | Numbers |
|---|---|
| Under 30 | 2 |
| 30–39 | 13 |
| 40–49 | 34 |
| 50–59 | 43 |
| 60–69 | 19 |
| 70–79 | 7 |
| Unknown | 1 |

Male 96 (81 %) Female 23 (19%)

The sex distribution is more like that for duod that for gastric ulcer The average length of histor and the average age at onset of dyspepsia was about

*The fact that concomitant* ulcers are co gastrectomy specimens than at necropsy co expected to have struck the pathologists duodenal lesion is often unrecognisable as before it leaves the operating theatre Many removed for a duodenal ulcer which is obv surgeon at laparotomy is later reported " severe antral gastritis but no ulcer "

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* This investigation was begun in 1948 during the tenure of a [illegible] ulme research scholarship from the Royal College of [illegible]ons

E II—ORDER OF APPEARANCE OF THE LESIONS

| — | Numbers | |
|---|---|---|
| evidence of either ulcer | 6 | [illegible] |
| idable evidence of position of first ulcer | 26 | 24 |
| of gastric ulcer found first | 6 | [illegible] |
| of duodenal ulcer found first | 79 | 60 |
| | | |

## The Present Series

ng my own 311 patients operated upon for peptic 9 (9%) have had lesions of both stomach and um 1 in 7 duodenal ulcer patients has also had r ulcer and 1 in 4 gastric ulcers has been associated duodenal one

lin (1954), in a longer series has observed similar ions though in other published series of operation here figures for concomitant ulcers have been ey have varied widely and have commonly been 1 in 20, corresponding with what may be the true nce as shown by the earlier post-mortem data , indeed in a large series of gastrectomies the ion of double lesions may be regarded as an index verage severity of the cases referred to the surgeon ed

he purpose of this investigation my own group ases has been supplemented by a further 90 vailable to me by my colleagues Sex and age tion were as shown in table I

*f Appearance of the Lesions* (table II)

cases both the duodenal and gastric lesions were when the patient was first investigated (or if radiographs had been taken these could not ed) In 6 cases radiography never showed either nd there was no dependable evidence as to which veloped first

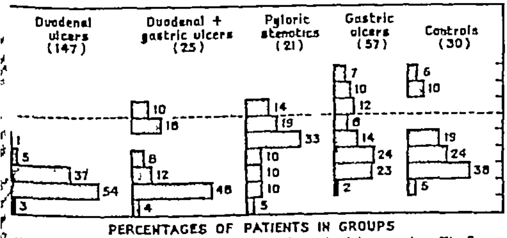
of the remaining 85 cases the duodenal ulcer was red first, either by X ray examination or because rated Review of early X ray pictures on which e ulcer was reported has not been possible in all ut 43 have been reconsidered in the light of later ments and no hint of a gastric ulcer has been n any of them

nly 6 patients was the gastric ulcer detected by aphy before any suggestion of duodenal ulcer served Reappraisal of the pictures in these cases d the appearances of absolute normality of the al cap in none though the irregularities were small ght well have been thought unconvincing In 5 e cases an old healed duodenal scar was found at on

tients (18%) had had perforations in the past and e had been duodenal

*n Pattern*

it is patients of the duodenal ulcer type and not of the gastric ulcer type who develop combined ulcers would be expected from the fact that it is usually if not always the duodenal ulcer which appears first This is further confirmed, however by secretion investigations The majority of those with two ulcers who were suitably investigated showed evidence of acid hypersecretion and in some cases this was gross (table III and fig 1) In a number of cases it was noticed that though the volume and total acidity of the juice was high, free acid was low or absent, signifying a large degree of intragastric buffering This is characteristic of gastric retention and conformed with my observation that pyloric stenosis had been a feature of many of my own cases of concomitant ulcers



icrogrammes of ionised hydrogen in whole of gastric night secretion. The figures e concomitant-ulcer group are seen to lie between those for duodenal ulcer and loric stenosis

### *Gastric Emptying*

At fluoroscopic observation of gastric emptying it is seen that barium passes through the pylorus ahead of each wave of peristalsis, and that this happens whether or not these waves meet across the lumen of the antrum But when they do not do so it is evidently impossible for them to exert much pressure and the pressure gradient required to cause the barium to pass through the pylorus must be produced mainly by a difference in tone between stomach and duodenal cap As the wave of peristalsis reaches the duodenal cap and begins to affect it the pylorus closes and the cap contents are therefore forced on into the rest of the small bowel The mechanism is not unlike that of the heart—the stomach resembling a giant auricle the duodenal cap behaving like a little ventricle going into systole and diastole and the pylorus taking the place of the mitral valve

TABLE III—ACID SECRETED AT NIGHT

| Milli-equivalents free HCl in bulked all night juice | Percentages in groups | | | | |
|---|---|---|---|---|---|
| | 170 D U | 25 D G U | 30 Pyl st | 80 G U | 30 Controls |
| Achlorhydria | 0 | 24 | 30 | 42 | 40 |
| 0–9 | 30 | 16 | 23 | 40 | 17 |
| 10–19 | 27 | 24 | 20 | 5 | 7 |
| 20–29 | 14 | 20 | 10 | 6 | |
| 30–39 | 8 | 4 | 3 | 4 | |
| 40–49 | 9 | 8 | 3 | [illegible] | 3 |
| 50–59 | 3 | | | 1 | |
| 60–69 | 1 | | | | 3 |
| 70–79 | 3 | | 3 | | |
| 80–89 | 2 | 4 | 7 | | |
| 90–99 | 1 | | | | |
| 100–109 | 1 | | | | |
| 110– | 1 | | | | |

D U = duodenal ulcer G U = gastric ulcer
D G U = duodenal and gastric ulcer Pyl st. = pyloric stenosis

Patients with concomitant gastric and duodenal ulcer are seen to have secretion patterns between those of patients with duodenal ulcers and those of patients with well-established pyloric stenosis and less like that of patients with gastric ulcers

From these observations it is not unreasonable to argue that an ulcer or scar involving the pylorus or any part of the duodenal cap is bound to reduce the efficiency of gastric emptying to a greater or lesser degree It is well known that duodenal ulcers occur in persons whose stomachs show excessive vigour and activity of all kinds muscular as well as secretory and that before an ulcer becomes established they display rapid gastric emptying Initially the exaggerated gastric tone may compensate for incomplete cap diastole due to scar but later the gastric emptying becomes slowed entering first the range regarded as normal and then that classed as gastric retention

### *Gastric Retention*

Pyloric stenosis and chronic gastric dilatation having been noted in a number of cases of concomitant ulcers retro spective analysis of all the others from this point of view was next undertaken

In 36 cases this was unrewarding Though even a small duodenal lesion may slow down gastric evacuation markedly, quite a large and callous one may give no certain evidence of having done so Many of these 36 patients had complained of vomiting and fullness during attacks, but none had reported regular and copious vomiting, none had been noted to have evidence of a dilated stomach or a succussion splash, and of none did the radiologist happen to have estimated the emptying-time For what it is worth, 29 of the 36 had had gruel or histamine test-meals, and these showed to a greater or lesser extent the "climbing" type of curve said to indicate gastric retention

In the remaining 76 patients (64%) there was incontrovertible clinical and radiological evidence of gastric retention, and in 39 (33%) well-marked pyloric stenosis was found and remarked upon at operation

Thus 64% of the patients with concomitant ulcers unquestionably had gastric retention, and most of the rest may have had it

The notes of all adult patients who had been in the Royal Free or Hammersmith Hospitals with pyloric stenosis during the past ten and past sixteen years respectively were now reviewed This diagnosis had been recorded for 331 patients and of these 52 (16%) had also had gastric ulcers, either found at radiography or discovered at operation or necropsy Some (1 in 5) of the latter had not been revealed by X-ray examination, and it is notorious that gastric ulcers are more difficult to demonstrate radiologically when there is pyloric stenosis and gastric retention When only patients who underwent surgery or who came to necropsy are considered the proportion of those with gastric ulcers rises to 19%

The evidence suggests that in at least 2 out of 3 cases of concomitant ulcer gastric retention is a main cause of the ulcer, and that of every 6 patients admitted to hospital with pyloric stenosis a gastric ulcer has already developed in 1 One is naturally led to question whether the slow rate of gastric emptying associated with this disease may not be a factor in the ætiology of all gastric ulcers

*Operative Findings* (table IV)

91% of the gastric ulcers were active, many were huge, 10 were bleeding, and 1 was perforated as well as bleeding

TABLE IV—FINDINGS AT OPERATION (110 CASES)

| Duodenal ulcer | Gastric ulcer | Numbers | % |
|---|---|---|---|
| Healed | Healed | 3 | 3 |
| Active | Healed | 6 | 5 |
| Active | Active | 26 | 24 |
| Healed | Active | 75 | 67 |
| Stenosis | Active | 32 | 29 |
| Stenosis | Healed | 1 | 1 |

The most frequent combination found (67%) was that of an active gastric ulcer and a healed, scarred, often stenosed duodenal lesion Both ulcers were active in 22%, both were healed in 5%, and in the remaining 6% an active duodenal ulcer was associated with one or more scars on the stomach The great frequency of healed, scarred duodenal lesions conforms with the other evidence that this is the older lesion Just as clinical pyloric stenosis is more often seen in patients with old healed ulcers than with open ones, so gastric ulcers are seen more frequently in association with healed than with active duodenal lesions

*Further Evidence from Additional Special Cases*

In 2 cases of gastric ulcer no sign of old duodenal ulcer was seen but the pyloric ring was observed to be ly thick and tight The specimens were

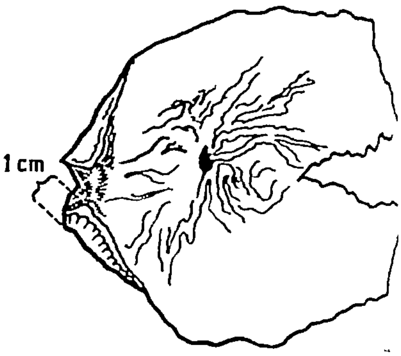


Fig 2—Three-quarters of a stomach resected for chron
The specimen shows the ulcer and massive ,
of the pylorus which had the feel of cartilage. (In a
specimen this degree of thickening would not, of
remarkable.) (Tracing of a photograph)

considered to be instances of adult hypertroph
stenosis (fig 2)

6 cases have been collected in which gastr
tomy had been performed some years ago for d
ulcers and in which recurrent ulcers had occ
ther surgery All patients were found to hav
ulcers, all had old scarred duodenums, 3 had
jejunal ulcers and 3 were observed to have
narrowed stomas and dilated stomachs.

Another patient had been submitted to gastr
tomy for duodenal ulcer in 1947 In 1949 this
undone Four months later I performed an
gastrectomy for a bleeding gastric ulcer and a
duodenum was observed The stomach disten
blood was unusually large This patient had ble
times

Having begun to suspect that pyloric
cause a gastric ulcer and having observed the
with which prolonged gastric retention follows
tomy, I wrote in 1947 "the author believes hyp
to be a main ætiological factor in a proportion
to the left of the angulus It may well be th
ulcer will prove to be one of the late compli
vagotomy in man" (Johnson 1948) Since the
choly prediction, a number of such ulcers
vagotomy have been reported and 4 have com
my own experience All 4 patients had healed
ulcers with much scarring, and all 4 had gross
gastric emptying and greatly dilated stomachs.

It might be thought that the acid h
characteristic (as is seen) both of patients with
ulcers and those with concomitant ulcers was
in the ætiology of the gastric ulcer, and indeed
be so However one final case may show that
an essential one, for this patient had a carcino
antrum obstructing the pylorus, a benign gast
proximal to it, and achlorhydria

## Peptic Ulcer and Hiatus Hernia

The association of peptic ulcer with hiatal h
now well recognised (Belsey 1952) Harrington
coincident gastric ulcer to friction on the lesser
of the stomach as it passes back and forth
margin of the œsophageal hiatus of the d
The coexistence of duodenal ulcer has
explained.

In a series of 30 patients with hiatal herni
met 4 with gastric ulcers, 4 with duodenal ulcers
with both a gastric ulcer and a healed, scarred d
ulcer, and this association can be linked w
has emerged concerning concomitant ulcers.

Hiatal hernias are of two main kinds—rolli
œsophageal and sliding or "short œsophagus ty
latter is associated with reflux œsophagitis, di

y and by œsophagoscopy, the former is usually

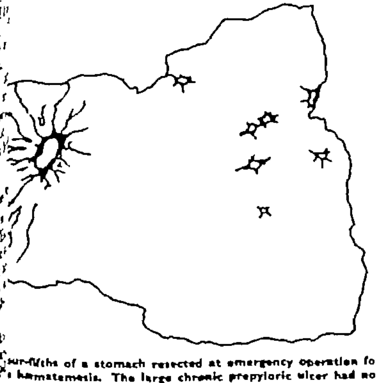
hiatus hernia is supposed to undermine the nce of the œsophago-gastric valve or sphincter nerally thought to be the cause of the reflux gitis. For a number of years the shortness of the gus and the accompanying thoracic stomach were d as congenital anomalies. But a congenitally d organ ordinarily draws its blood-supply from y source; indeed the short, tight vessels often surgical alteration of its position Such a state is not seen in hiatus hernia and on one occasion ble to reduce with ease at operation a hernia in he whole stomach and most of the transverse ccupied the right side of the chest It is now y accepted that most if not all short œsophaguses uired

ctically three groups of factors could contribute ation of a hiatus hernia; those which relax the of the hiatus in the right crus, those which affect sure gradient between abdomen and thorax, and hich control tone in the longitudinal muscle of phagus In the rolling type of hiatus hernia in he cardia remains below the diaphragm evidently e first two factors can have operated. In the type I believe œsophageal spasm to be paramount observed for 4½ and 5½ years, two patients ll marked reflux œsophagitis in whom hernias ly absent, have recently appeared and enlarged erefore hold that, in at least a proportion of cases g hiatus hernia incompetence of the œsophago valve or sphincter is the first cause, and reflux gitis with œsophageal spasm the second cause of iation

athognomonic symptom of reflux œsophagitis is rn This symptom is common in duodenal ulcer n indicates that there is reflux into the gullet of e often the excessively acid gastric contents The retention which characterises active duodenal the probable cause of this tendency to œsophageal But if reflux œsophagitis can cause hiatus hernia ested, the likely reason for the occasional dis of duodenal ulcer and hiatus hernia together is t.

ic retention has been shown sometimes to result stric ulcer and I suggest that in some cases of nt gastric ulcer and hiatus hernia gastric retention h the predisposing cause of both

y own series of hiatus hernias of the short gus" type evidence of delay in gastric emptying n found in 47% including all 9 cases in which ere coincident peptic ulcers



ur-fifths of a stomach resected at emergency operation for hæmatemesis. The large chronic prepyloric ulcer had not it had caused pyloric obstruction by scar *The hæmorrhage* om acute gastric ulcers several of which contained blood-clot, were impalpable from outside the stomach. (Tracing of a aph.)

## The Prognosis in Combined Ulcers

With coexisting gastric and duodenal ulcers, the risk to the patient is greater than the sum of the risks from either ulcer alone Hæmorrhage specially from the gastric ulcer is common in all 10 patients in my series who were admitted to hospital actively bleeding, the blood came from the gastric ulcer Of the patients with gastric ulcer alone admitted during the same period to the hospitals from which the series of concomitant ulcer is drawn 8% had bled at some time in the past but among those with concomitant ulcers no less than 47% had at some time had major hæmorrhages and 20% had had several.

In an analysis of 3000 post-war elective gastrectomies which forms part of a separate study the over all mortality was found to be 4% The death rate among those with combined ulcers was 10% and this was not attributable to a difference in age distribution In the present series of 119 cases there were 12 deaths in hospital

## Treatment

In the treatment of patients with combined gastric and duodenal ulcers it is important to bear in mind two facts

(1) An element of gastric retention is almost certainly present and this indicates special preoperative measures, such as gastric decompression and lavage and particular attention to likely depletion of water electrolyte, and protein reserves

(2) The patient is of the duodenal ulcer type and likely to be capable of acid hypersecretion, even though this is not always evident in the presence of pyloric obstruction I have often advocated moderate resection for gastric ulcers in the belief that, since hypersecretion is not a feature of these patients, radical resection is unnecessary provided that all diseased tissue is removed (Johnson 1950, Johnson and Orr 1954) For combined ulcers, however as for duodenal ulcer, *an operation adequate to control hypersecretion must be performed*

When a patient is operated upon for urgent hæmorrhage and evidence of a duodenal ulcer is seen it should not be assumed that this is the source of the hæmorrhage particularly if the duodenum is much scarred for in such a case there is a substantial chance that the bleeding is coming from a concomitant gastric ulcer sometimes as in 3 of my cases an impalpable one (fig 3)

Patients with gastric ulcers who have symptoms such as heartburn or vomiting should be suspected of gastric retention and should be especially investigated from this point of view

The reason why sleeve resections for gastric ulcer were followed by recurrences is I suggest that gastric retention followed the denervation of the distal part of the stomach and the pylorus

It is now often stated that though gastrectomies for duodenal ulcers may occasionally be followed by stomal ulcers, recurrences after resection for gastric ulcers are almost unknown However though I favour and have had good results with Billroth I gastrectomy for gastric lesions I predict that its present widespread revival and popularity will lead to recurrent gastric ulcers due to its use in some unsuitable cases where the creation of only small and inadequate stomas has been possible

Finally I would urge that concomitant gastric and duodenal ulcers are too dangerous to warrant non operative management and that surgery should be resorted to early before the risks become excessive

## Summary

Gastric and duodenal ulcers occur in quite different sorts of people The question therefore arises why ulcers should sometimes be found in the stomach and the duodenum of the same patient

The incidence of concomitance of duodenal and gastric ulcers is probably about 5% if symptomless ulcers are included Of ulcer patients who come to hospital for

investigation about 7% have both duodenal and gastric lesions Surgeons, however, commonly see a greater proportion of such patients, and there were 9% in a surgical series of 311 cases

Analysis of a series of 119 cases of concomitant ulcers yielded the following facts

1 The duodenal ulcer is the first to appear

2 The patients have a secretion pattern which lies between that of patients with duodenal ulcer and that of patients with established pyloric stenosis It is much less like the secretion pattern of gastric ulcer patients

3 A substantial majority of patients with concomitant ulcers have gastric retention and many have gross pyloric stenosis Some 16% of patients admitted to hospital with pyloric stenosis have gastric ulcers as well.

4 At operation the commonest finding is an active gastric ulcer and a healed, scarred duodenal one

12 additional cases are described which illustrate how gastric retention from causes other than duodenal ulcer may also be complicated by the development of gastric ulcers

9 cases are reported of peptic ulcers associated with hiatus hernia It is suggested that reflux œsophagitis may sometimes cause hiatus hernia (instead of vice versa) and reflux may in turn be caused by duodenal ulcer and gastric retention Gastric retention may also apparently cause gastric ulcer, and the association of these lesions may be thus explained

Patients with concomitant ulcer are particularly prone to have hæmorrhages, and when they do it is usually the gastric ulcer which bleeds

Once concomitant ulcers have become established, elective surgery is four times more dangerous than in cases of solitary ulcers

The bearing of these observations upon the treatment of patients with concomitant gastric and duodenal ulcers is discussed

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# RADIOTHERAPY OF CUSHING'S SYNDROME

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It is now well established that the signs and symptoms of Cushing's syndrome are caused by adrenal cortical overactivity This may be due to an adrenal cortical tumour, but bilateral cortical hyperplasia is more commonly found, and it is widely thought that this is due to increased pituitary adrenocorticotrophic activity

When no tumour can be found, treatment of the syndrome may be directed either at reducing the amount of cortical tissue by surgery or at diminishing the stimulus to cortical overactivity by irradiation of the pituitary gland

Unilateral adrenalectomy does not usually influence Cushing's syndrome significantly (Sprague 1953), but bilateral subtotal adrenalectomy and total adrenalectomy, developed at the Mayo Clinic by Priestley et al (1951) has produced excellent remission of symptoms in nearly al[illegible]ts But this operation is a considerable under-[illegible]n in skilled hands, and is often followed by chronic adrenal insufficiency, which requires treatment with cortisone

Further evidence is presented here that the p Cushing's syndrome may be arrested, and that able improvement may take place in suitable after irradiation of the pituitary gland This is simple, involves no operative risk and is not by chronic adrenal insufficiency 6 patients the last five years are reported, details of the used are described, and the assessment of is discussed

The difficulties of excluding the presence of a cortical tumour are again emphasised, but can be achieved, radiotherapy should be used initial treatment If this does not arrest or the condition, surgery may still be undertak with undiminished chances of success

## Material

The 6 patients (table I) were all females age They presented most of the features desc Cushing (1932), and additional evidence of corti function was obtained by estimation of the excretion of corticosteroids and neutral 17 ke and by measuring glucose tolerance. Cortic (formaldehydogenic) were measured by the m Corcoran and Page (1948), the normal range women in our laboratory being 0 3–0 8 mg in four hours Neutral 17-ketosteroids were mea the method recommended by the Medical Council (1951) The normal range for adult 6–18 mg in twenty-four hours Well marked and much-increased excretion of androgens an adrenal cortical tumour were not observed, there any evidence of a tumour on clinical or ra examination

TABLE I—DETAILS OF SIX CASES OF CUSHING'S S

| Case no | Age (yr ) | History | Weight (lb ) | Striæ | Hirsuties | Polycythæmia | Amenorrhœa | Blood pressure (mm Hg) | Glucos tol rance |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 28 | 10 yr | +70 | + | + | + | 7 mos | 180/105 | Diabet |
| 2 | 23 | 3 yr | +20 | + | + | + | 8 mos | 160/100 | Reduce |
| 3 | 36 | 5 yr | +28 | + | + | – | 12 mos | 210/130 | Diabet |
| 4 | 33 | 1 yr | +7 | + | + | – | 11 mos | 220/150 | Reduce |
| 5 | 23 | 6 mos | + | + | + | – | 4 mos | 150/100 | Normal |
|  | 34 | 2 yr | +42 | + | + | – | 2 yr | 160/120 | Reduce |
| 6 | 19 | 3 yr | +29 | + | + | – | 2½ yr | 170/115 | Normal |

One of the patients had been previously trea radiotherapy for Cushing's syndrome and, af years' remission, a relapse following pregnancy further treatment

## Treatment

Deep X-ray therapy was given to the pituit with a high-voltage unit (250 kV peak, half va 1 75 mm of Cu) Six circular beams of X ray focal skin distance were directed at the pitui with the aid of a plaster shell through portals around the hair line A maximum dose of was given in twenty eight to thirty days, the skin dose being about 3000r Larger doses are inadvisable because of the possible developme cortical atrophy

Reducing diets were used to control obes necessary, but no other treatment was given

## Results

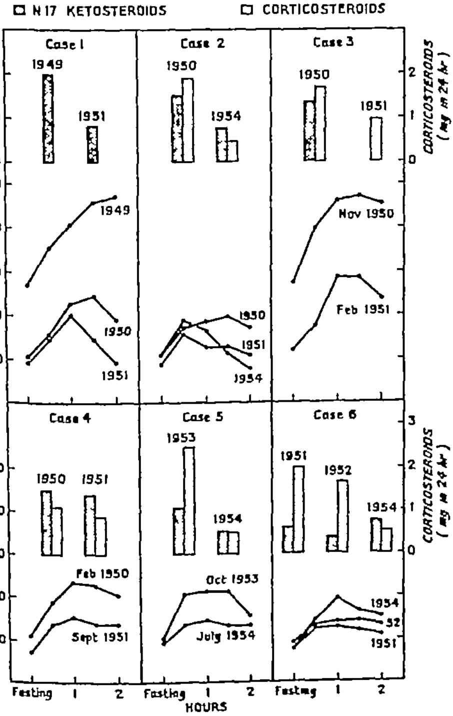
In assessing progress after treatment the factors were studied (table II) (1) the general ance, (2) the texture of the skin and the app

TABLE II—RESULTS OF TREATMENT

| Date | Weight (lb) | Blood pressure (mm.Hg) | Menstruation | Glucose tolerance | Cortico steroids (mg in 24 hr) | 17 Keto steroids (mg in 24 hr) | Irradiation (r) | Result |
|---|---|---|---|---|---|---|---|---|
| 1949 | 199 | 180/105 | Absent | Diabetic | | 30·80 | 5600/5100 | Remission |
| 1954 | 192 | 120/80 | Regular | Normal | | 10·60 | | |
| | | | | | (1951) | | | |
| 1950 | 158 | 150/100 | Absent | Reduced | 1·90 | 30·50 | 5200/4700 | Remission |
| 1954 | 147 | 120/70 | Irregular | Improved | 0·80 | 15·60 | | |
| Dec 1950 | | 210/130 | Absent | Diabetic | 1·68 | 20·30 | 4500/3700 | Died of cerebral hæmorrhage |
| pr., 1951 | | 165/100 | Absent | Improved | 0·96 | | | |
| 1950 | 124 | 230/160 | Absent | Reduced | 1·00 | 29·80 | 4100/3900 | Remission |
| 1951 | 124 | 150/105 | Regular | Improved | 0·90 | 25·00 | | |
| | | | | | (1951) | | | |
| 1943 | 160 | 150/100 | Absent | Normal | | 18·00 | 1700/1550 | Remission |
| 1944 | 171 | 120/85 | Regular | | | | | |
| 1953 | 184 | 160/120 | Absent | Reduced | 2·50 | 21·60 | 3000/2873 | Remission |
| 1954 | 168 | 140/100 | Irregular | Improved | 0·18 | 10·00 | | |
| 1951 | 134 | 170/115 | Absent | Normal | 1·99 | 12·00 | 4000/3400 | Not progressive |
| 1952 | 141 | 130/100 | Regular | | 1·64 | 7·37 | | |
| 1954 | 134 | 140/100 | Irregular | | 0·53 | 14·80 | | |

m (3) the menstrual history (4) urinary n of steroids (5) glucose tolerance and (6) ressure

f the 5 surviving patients there was considerable ment The 5th patient showed only temporary ment, but her disease has not progressed since nt three years ago



n tolerance and urinary excretion of steroids before and after treatment.

One patient died of a cerebral hæmorrhage five months after treatment was completed; she had had hypertension for many years and a vascular accident five years previously but before her death there was evidence of improvement in her Cushing's syndrome Necropsy showed mild enlargement of both adrenal cortices and hyaline changes in the pituitary basophil cells but no adenoma was discovered.

Treatment led to slow but continued improvement diminishing plethora and fading of the skin striæ usually becoming evident one to three months after the start of treatment Polycythæmia present in 2 patients disappeared during this period Hirsuties was less influenced and remains prominent in 2 patients who are otherwise normal

Menstruation became re established after a variable time in all the surviving patients but ceased again in case 6 and remains irregular in cases 2 and 5 Glucose tolerance curves showed improvement in all cases where it had been abnormal Case 1 with an originally diabetic type of curve now shows normal glucose tolerance despite failure to observe any dietary restrictions her weight remaining substantially unchanged Significant improvement was observed in the remainder (table III)

The urinary excretion of corticosteroids diminished in 4 patients but in a 5th who is clinically well the change was slight and excretion remained at the upper limit of normal The urinary excretion of 17 ketosteroids which was moderately increased in 5 patients showed significant reduction in only 2 patients

The blood pressure fell in all the patients but in only 2 did it fall to normal levels When hypertension had been present for a long time and secondary changes had taken place in the kidneys and blood vessels as in case 3 this outcome was to be expected

## Discussion

When a patient presents the appearance of Cushing's syndrome it is important to establish that this is due to adrenal cortical overactivity Obesity and hirsuties occur with hypertension and irregular menstruation in women as a constitutional abnormality The condition is not progressive and evidence of cortical overactivity is absent

No single clinical feature of Cushing's syndrome can be regarded as pathognomonic or essential to the diagnosis Although we have found the skin changes a reliable clinical indication, we have confirmed the presence of cortical overactivity by the estimation of urinary excretion of corticosteroids Absolute eosinophil-counts and the urinary uric acid creatinine ratio were not used, but additional evidence was forthcoming in some patients who showed diminished glucose tolerance and increased urinary excretion of neutral 17 ketosteroids

The presence of cortical hyperfunction having been established it is necessary to determine whether this is due to a cortical tumour A short history with rapid development of symptoms and well marked changes in the sexual sphere suggest that a tumour is present Much increased urinary excretion of androgens with an increase in the β-ketosteroid fraction may provide confirmatory evidence. In men showing well-marked feminising changes tumours are almost invariably present, and excessive excretion of œstrogen was found in 1 such case by Simpson and Joll (1938)

Clinical examination rarely reveals the presence of tumours, but they may sometimes be demonstrated by plain radiograms, pyelography, or peri renal insufflation of air Sprague (1953) points out that the tumours causing Cushing's syndrome may be very small and impossible to demonstrate radiographically In his cases tests of urinary excretion of steroids proved unreliable in distinguishing tumour from hyperplasia, and he therefore advocates exploratory operation as the only certain method of making the distinction A functional adrenal cortical tumour is associated with atrophy of the opposite adrenal gland, either of these situations being readily recognised at operation by an experienced surgeon

On the other hand, patients with long and slowly progressive histories, prominent metabolic disturbances, and little evidence of virilism are more likely to have adrenal cortical hyperplasia In these patients the excretion of corticosteroids is always considerably increased, but the excretion of 17 ketosteroids is only slightly increased and may be within normal limits Surgical exploration in these cases reveals either normal-sized or enlarged glands on both sides

The prognosis in Cushing's syndrome is poor, about half the patients dying within five years of the establishment of the diagnosis (Plotz et al 1952, Sprague 1953) Intercurrent infection, the effects of hypertension, osteoporosis, and psychological changes contribute largely to the morbidity of Cushing's syndrome In the remainder spontaneous variations in the activity of the syndrome are common, deterioration is slower and punctuated by remissions, the final prognosis depending on cardiovascular and renal changes resulting from the hypertension characteristic of the syndrome

The value of treatment is difficult to assess because of these spontaneous variations in activity and because numerous different forms of treatment have often been used in published cases It is important that progress should be adequately followed and objective evidence of improvement obtained before good results are claimed from a particular form of treatment Until recently the treatment leading to remissions in the highest proportion of cases has been irradiation of the pituitary gland Widely different techniques of treatment and dosage have been used, with variable results in different clinics, and Sosman (1949) found that only 38% of all patients treated in this way had improved Of his own 6 cases, however, 4 showed considerable improvement after radiotherapy

The serious prognosis, high morbidity, and unreliable results of previous forms of treatment in Cushing's syndrome encouraged Priestley et al (1951) to attack the condition at the adrenal level by surgical means At operation the presence or the absence of an adrenal cort[illegible] tumour can also be most satisfactorily decided When neither tumour nor atrophy (indicating of the opposite adrenal gland) is found, the recommend removal of nine-tenths of one a and complete excision of the opposite one.

This treatment is quite logical and strictly to the treatment of hyperthyroidism by subtotal ectomy Although there have been a few re of their 48 surviving patients are in rem likelihood of chronic adrenal insufficiency operation is great, and its potential dangers more serious than those of myxœdema afte ectomy Half these patients are receiving su treatment with cortisone (Sprague 1953)

Substantial improvement has resulted in 4 patients treated by the method described her considered that controlled Cushing's syn preferable existence to controlled adrenal and that radiotherapy should be used before is contemplated If this fails to arrest the p Cushing's syndrome within six to twelve months treatment can then be used with undiminished of success

## Summary

6 cases of Cushing's syndrome treated by irradiation are reported

Considerable objective improvement result of the 6 cases

Pituitary irradiation is preferable to surg initial treatment of Cushing's syndrome due to cortical hyperplasia

I wish to thank Dr H Gardiner Hill, under whose patients were admitted to hospital, and Dr W J Gr undertook the biochemical investigations, for per publish and for much helpful criticism and adv Dr I. Churchill-Davidson for details of the tech in irradiating the pituitary gland

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# CONTINUOUS MURMURS WITHO PATENT DUCTUS ARTERIOSU

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Seven cases of patent ductus arteriosus atypical murmurs were heard and the usual c machinery murmur was absent were rep Bonham Carter and Lovel (1953) As a direct to this we report here five cases in which a c murmur was heard in the pulmonary area in th of any of the usual causes of such a murmur, patent ductus arteriosus Four of these child subjected to thoracotomy, and two of the with the fifth case) came to necropsy The a patent ductus was thereby definitely excluded

## Case-reports

The main clinical features of the five cases are in tables i and ii The remaining points of in as follows

TABLE I—CLINICAL FEATURES

| se no | 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|
| y and labour | Normal | Normal | Normal | Normal | Normal |
| ght | 6 lb 12 oz | 8 lb 6 oz | 9 lb 12 oz | 6 lb | 6 lb |
| murmur was d (mos.) | 9 | 10 | 6 | 3 | [illegible] |
|  | Present | Present | None | Variable | Present during infancy |
| ght | Yes | Yes | No | Yes | Yes |
| es | Normal | Normal | Normal | Normal | Delayed |
|  | None | Present | ? Present | Present | ? Present |
| eranco | Fair | Poor | Poor | Poor | Poor |
| ry illnesses | Present | Present | Present | Present | Present |
| <br>nary<br>t | Systolic<br>Systolic and diastolic<br>Systolic | (Systolic and diastolic at left sternal edge)<br>Systolic | Masked by chest sounds | Systolic | Systolic<br>Systolic and diastolic<br>Systolic |
| <br>nary<br>: | None<br>Continuous<br>Systolic and diastolic | Diastolic<br>Continuous pulmonary and systolic at left sternal edge<br>None | Systolic<br>Continuous<br>None | Diastolic<br>Continuous<br>None | Systolic<br>Continuous<br>Systolic and diastolic |
| rdiogram<br>r<br>r | Left ventricular hypertrophy<br>? Right ventricular hypertrophy<br>Right bundle-branch block | Left ventricular hypertrophy<br>Right ventricular hypertrophy<br>Right bundle branch block | Left ventricular hypertrophy<br>Right ventricular hypertrophy<br>Changes in P and T waves | Right ventricular hypertrophy<br>Right bundle branch block | Left ventricular hypertrophy and strain |
| atheterisation<br>s | Ventricular septal defect<br>Right hypertension |  |  | Suggested patent ductus | Suggested patent ductus |
| tive heart- | ± | Present | Absent | Absent | Absent |

1 —A girl born on March 24 1948 in whom a murmur ected at the age of 9 months, was referred to the tal heart clinic about a year later She contracted g-cough at the age of 1 year and pneumonia at the years and had several attacks of bronchitis There relevant family history She was admitted with and radiological signs of collapsed right lower lobe

*ac investigations* after her recovery from this condition ed the presence of a patent ductus arteriosus and stenosis with incompetence Cardiac catheterisation the presence of a ventricular septal defect with a ntricular pressure of 58 mm Hg

*tion* —A patent ductus arteriosus being suspected an tory thoracotomy was done but the child died during ration.

*opsy findings* (table III) included ventricular septal endocardial fibro-elastosis aortic stenosis and incom mitral stenosis, and congestive cardiac failure ted with the last of these were pulmonary oedema, ion, and collapse and cerebral oedema General lymphoid hyperplasia hydromyelia of the cervical cord and mild infection of the upper respiratory tract were also found.

BLE II—SALIENT FEATURES OF PATENT DUCTUS

| Case no | 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|
| g pulse | 0 | + | + | 0 | + |
| lse-pressure | + | + | + | 0 | + |
| ous murmur | + | + | + | + | + |
| enlargement<br>ventricle<br>ventricle | + +<br>+ +<br>+ | + +<br>+<br>+ | + +<br>+<br>+ | +<br>+<br>+ | + +<br>+ +<br>+ |
| ry plethora | + | + | ± | + | 0 |
| ary second sound | + | + | Normal | + | + |
| ardiogram showing left cular hypertrophy | + | + | + | 0 | + |

Case 2 —A girl born on Dec 27 1951 There was no relevant family history A murmur was heard during examination because of gastro-enteritis at the age of 10 months She was not seen at Great Ormond Street till March 13 1954 when she was referred to the congenital heart clinic At this age (27 months) she could not walk and was having most of her food by bottle There was nocturnal dyspnoea; she was constipated and losing weight She was admitted in congestive failure and was given digoxin and sedatives. She responded slowly and later investigation suggested the presence of a patent ductus arteriosus and possibly aortic stenosis

*Operation.*—At thoracotomy a coarse thrill was found in both the pulmonary artery and the aorta but the ductus was sclerosed Left auricular biopsy proved the presence of endocardial fibro-elastosis and lingular biopsy showed pulmonary hypertensive vascular changes. This hypertension was also proved by the intracardiac pressures recorded at operation: right auricle 15/10 mm Hg right ventricle 74/16 mm Hg pulmonary artery 81/58 mm. Hg left ventricle 108/23 mm. Hg and aorta 109/5- mm. Hg

*Postoperatively* the patient's condition became critical Congestive failure increased despite digoxin morphine oxygen and mercurial diuretics, and she died on the eighth postoperative day

*Necropsy* revealed a large ventricular septal defect widespread endocardial fibro-elastosis involving the mitral valve dilatation and hypertrophy of all the heart chambers probe patency of the foramen ovale and postoperative fibrinous pericarditis. There was also visceral evidence of congestive cardiac failure and hydromyelia of the lumbar cord

Case 3 —A boy born on March 4 1952 There was no relevant family history Symptoms of breathlessness wheeziness and difficulty in feeding had been present from birth and he was admitted to Great Ormond Street at the age of

TABLE III—PATHOLOGICAL AND CLINICAL FINDINGS

| entricular septal defect | Aortic valve | Mitral valve | Pulmonary valve | Congestive cardiac failure | Endocardial fibro-elastosis | Miscellaneous |
|---|---|---|---|---|---|---|
| + | Stenosis, incompetence | Stenosis |  | + | + | Fenestration of pulmonary cusps |
| + | Opaque | Dilated<br>? Incompetence<br>cusp nodules | Dilated<br>? incompetence | + | + | Slight dextropositioning of aorta |
| - | Stenosis | Thickened cusps |  | + | + | Coarctation with large collateral |
| + |  |  | Incompetence<br>? stenosis | - | - | Pulmonary hypertension |
| + | Incompetence<br>? stenosis |  |  | - | - | Pericardial defect |

6 months A continuous murmur was heard by several observers and, in addition to other signs suggesting a patent ductus, his femoral pulses were absent and blood pressure was unrecordable in his legs He had severe bronchospasm, which responded well to ephedrine He was allowed home but returned a month later in extremis On his second admission there was clinical and radiological evidence of consolidation and collapse of the right upper lobe and severe bronchospasm He was given digoxin, oxygen, penicillin, and sedatives and, later because of his poor response, intravenous procainamide He still did not improve and, though intravenous aminophylline was also tried, he died about twenty four hours after admission The clinical diagnosis was coarctation of the aorta, patent ductus arteriosus, and cardiac failure precipitated by severe respiratory infection and bronchospasm

*Necropsy* confirmed the coarctation, congestive failure, and respiratory infection. There was no patency of the ductus, but endocardial fibro elastosis of the left atrium with thickening of the mitral and aortic valves was found There were also some intimal and elastic tissue changes in the coronary arteries and a very large collateral internal mammary artery

**Case 4** —A boy born on Feb 5, 1947 There was no relevant family history He was seen at Great Ormond Street about the age of 3 months because of frequent respiratory illnesses and was referred to the congenital heart clinic for cardiovascular investigation His cardiac enlargement was associated with considerable chest deformity, and he had, on most examinations, moist sounds in his chest He had no other evidence of congestive cardiac failure Cardiac catheterisation showed a higher oxygen saturation in the pulmonary artery than in the right ventricle and pulmonary hypertension (pulmonary artery 60/32 mm. Hg) These suggested a patent ductus

*Operation* —At thoracotomy right ventricular hypertrophy and a dilated pulmonary artery only were found Lingular biopsy showed hypertensive changes in the pulmonary vessels, and organising pneumonitis (probably viral in origin) was observed This latter finding adequately explained the persistent moist sounds in the chest

*Follow up* —When seen in August, 1954, the boy was fairly active, still had a trace of cyanosis, and still showed clinical and radiological evidence of collapse at his left base It was thought that the collapse might have been due in part to infection and in part to the gross cardiac enlargement He was readmitted in August, 1954, with a further respiratory infection, which responded well to antibiotics

**Case 5** —A girl born on Dec 22, 1942 There was no relevant family history Breathlessness on exertion without cyanosis had been observed since birth, and she contracted chickenpox, whooping-cough, and numerous attacks of bronchitis At the age of 2 years, during an attack of bronchitis, a cardiac murmur was heard, but she was not seen in the congenital heart clinic until the age of 8 years Although the pulmonary vasculature appeared normal on screening, there was a large pulmonary artery outline, and the other evidence suggesting a patent ductus was convincing (see table II) Finger plethysmograph and femoral artery tracings were inconclusive, but cardiac catheterisation revealed a high oxygen saturation in the pulmonary artery

*Operation* —At thoracotomy no ductus was found The left auricular appendage and pulmonary artery were seen to bulge through a defect in the pericardium (explaining the findings on radioscopy) Since discharge she has been having slight precordial pain suggesting angina but is otherwise very well The diagnosis was thus revised to a high ventricular septal defect, aortic stenosis and incompetence, and a pericardial defect

## Discussion

There are at least six well recognised causes of a continuous murmur heard over the precordium The best known is the Gibson or machinery murmur of a patent ductus arteriosus, which is loudest in the second or third intercostal space—over, or just lateral to, the pulmonary area Although the classical murmur sounds continuous on auscultation, the phonocardiographic tracing of the sound (fig 1) often begins in mid or late systole, rises to a crescendo at the second sound, and diminishes thereafter to end usually about mid-diastole The second sound is usually distinguishable in the midst

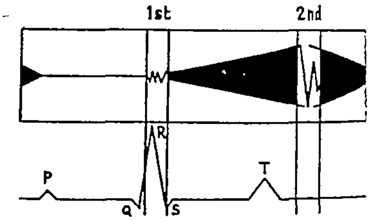


Fig 1—Phonocardiogram of typical murmur in a case arteriosus second left intercostal spac

of this murmur both by auscultation and b cardiography

The continuous hum of venous origin is mistaken for a ductus murmur, because it softer, and though more commonly right-sided heard up towards one or both clavicles an them It cannot be heard posteriorly, an unique in that it can be made to alter or to by turning the head or by digital pressure on in the neck

In cases of pulmonary atresia or persistent arteriosus the lungs may derive their blood-sup the aorta The anastomosis thus formed betw bronchial and the pulmonary vessels produce tinuous murmur This may be heard over an the chest Its point of maximal intensity is di locate but is not uncommonly posterior or in th It is usually a soft sound, uninfluenced by po or by venous pressure

Much less often the continuous murmur may over an arteriovenous aneurysm In anomaly is invariably congenital and may be The murmur may be heard in the axilla (Lu or over the aneurysm Equally unusual is the co

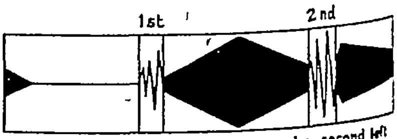


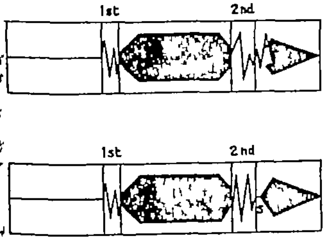
Fig 2—Outline of phonocardiogram in case 1 : second left space.

aortopulmonary communication, in which the audible over the base

The last two possibilities are even more rare foration of a sinus of Valsalva (aortic sinus) pulmonary artery or into the right ventricle by Wood (1950) as a cause of a continuous and (2) Taussig (1947) has heard such a murm case of congenital pulmonary stenosis and inco with associated anomalies of the aortic valves.

To this list must now be added the present Clinically these cases presented features strongly suggested patent ductus that thoracot done on four children, and a fifth died sudden he could be operated on Table II shows how the findings in these cases resembled those of a lductus, and in case 4 alone were there any ble grounds for doubt in this instance the d pulse-pressure were normal, and there was no rdiographic evidence of left ventricular hyper A normal electrocardiogram is commonly found of patent ductus, particularly in younger children 4, however, it is rather surprising in view of the cardiac enlargement

w of this difficulty in diagnosis to resolve which ory thoracotomy was undertaken an explanation e continuous murmurs should be sought In basal systolic and early diastolic murmur would uced by the aortic stenosis and incompetence ere originally diagnosed In the phonocardiogram nboid systolic outline of such a valvular stenosis ends about 0 04 sec. before the second sound continuity is present (Reinhold and Nadas 1954) tolic murmur of a ventricular septal defect (also in case 1) continues up to the second sound in ses It is conceivable that the superimposition sounds, together with those produced by fenes of the pulmonary valve cusps, would produce a indistinguishable from the continuous ductus on auscultation The phonocardiographic outline a combined sound might however differ slightly at of the ductus and in fact did so in case 1 sing a decrease of intensity of the murmur just he second heart sound The difference between ical patent-ductus murmur and the outline d in case 1 can be appreciated on comparing



asal diastolic murmurs: above silent period lost owing to of second component of second sound; below S indicates period.

and 2 This atypical outline has been observed r cases of patent ductus by Reinhold and Nadas but such an atypical tracing in cases with unusual features might be of some diagnostic value

2 is less easy to explain Endocardial fibro-elastic ing in the absence of damage to the valves, s no murmurs The ventricular septal defect be responsible for a long basal systolic murmur mid diastolic or even presystolic murmur at the but these could not produce a basal continuous

The other possibility is that the septal defect lmonary hypertension had enlarged the pulmonary o the extent of producing an incompetence murmur area Dilatation of the valve ring was found ortem. The trouble with this suggestion however, although murmurs due to incompetence heard at e are often early there may be a short silent period e second sound Wells et al (1949a) found that uarters of the basal diastolic murmurs had a cres liminuendo configuration (fig 3) but that a pure endo pattern is sometimes seen when the second nent of the second sound is delayed Whether t that most of the cases reported by Wells et al and b) were rheumatic in origin and not con is important or not it is impossible to say; but diastolic element in case 2 was due to pulmonary

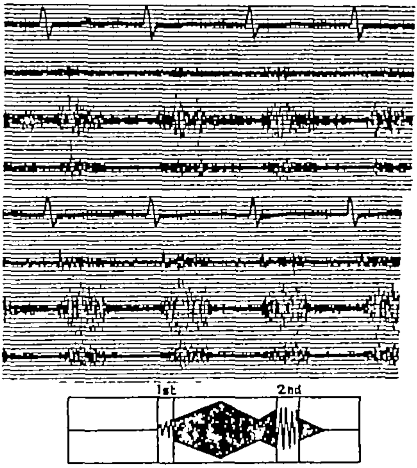


Fig. 4—Phonocardiogram in case 2: upper tracings second left intercostal space lower tracings, second right intercostal space.

insufficiency this case would have to be one of the 25% with pure diminuendo diastolic patterns (fig 3) The phonocardiogram of case 2 (fig 4) shows a rhomboid systolic configuration Although such a pattern is usually seen in valvular stenosis (see case 1) it has rarely been observed in cases of ventricular septal defect The continuous tracing is more obvious in the aortic area (see also case 5)

Case 3 is as difficult to explain The murmurs of aortic stenosis and coarctation could not produce a continuous sound over the base Precordial diastolic murmurs are sometimes heard in cases of coarctation of the aorta, but they resemble aortic insufficiency murmurs (Wells et al 1949b) These workers report the following interesting finding in six out of fifteen cases of coarctation "The diastolic vibrations were characteristically of decrescendo configuration being a continuation from the systolic murmur" This finding however was only observed when listening and taking tracings over the spine Mitral stenosis found post mortem in case 3 again raises the question of pulmonary incompetence as

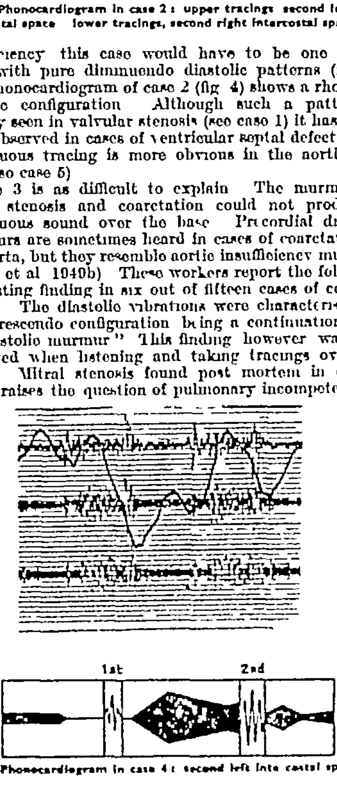


Fig 5—Phonocardiogram in case 4: second left intercostal space.

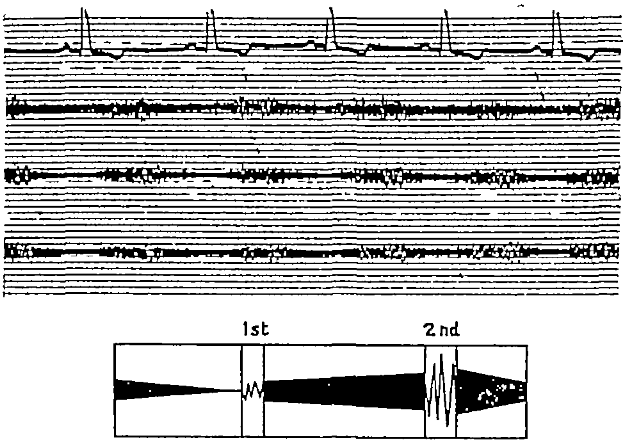


Fig 6—Phonocardiogram in case 5 second left intercostal space

a source of diastolic sounds, but much the most important alternative cause was a greatly dilated collateral internal mammary artery A continuous murmur is not infrequently heard on auscultation of the lactating breast, and it is known that the blood-flow through the internal mammary artery is greatly increased at such times Unfortunately no phonocardiogram could be taken from this child, because of the severe and persistent accompaniments in his chest

To explain the murmur in case 4 one must again assume that pulmonary incompetence produced an early diastolic murmur, and in this instance there is the suggestion of a short silent period (fig 5) The ventricular septal defect was proved by cardiac catheterisation and was doubtless responsible for the systolic element of the continuous murmur The complete outline (fig 5) was again atypical, showing much the same systolic outline as in cases 1 and 2

Case 5 closely resembles the first from the point of view of the phonocardiogram taken over the pulmonary area Fig 6 shows the aortic area tracing, which is quite typical of that of a patent ductus murmur Perhaps more importance should have been attached to this rather unusual finding Although the ductus murmur can often be heard to the right of the sternum, it is loudest (except in dextrocardia and cases of right aortic arch) to the left of the midline The finding of a high oxygen saturation in a high right ventricular sample on catheterisation might avoid the wrong diagnosis made in case 5 Although this finding would support the diagnosis of a ventricular septal defect it has been found in cases of patent ductus in which there is pulmonary regurgitation

The lesions detected clinically and post mortem are outlined in table III All the cases have multiple abnormalities, but a ventricular septal defect is common to all except one The cause of the murmur in this one exception might be the large internal mammary artery One is therefore probably justified in adding two further causes of continuous murmurs to those listed above complicated ventricular septal defect, and large tortuous collateral vessels

## Conclusion and Summary

An attempt has been made to explain a continuous murmur heard at the base in five cases of congenital heart disease None of these had the lesions which are recognised as causing such murmurs, and there is no way of further proving the accuracy of the explanations given It can be said, however, that in any case showing the features of a patent ductus arteriosus, and in which multiple lesions are suspected, a careful study of the phonocardiogram may be of some help In such cases causes of continuous murmurs should be born in mind complicated ventricular septal large tortuous collateral vessels

Intravenous angiocardiography does not al an answer and has its risks The greater ris grade aortography make it hardly justified at It is therefore likely that, in such difficult plicated cases as these, exploratory thor sometimes be done no matter how carefully are investigated Although the death rate is hi small series, it is considered that thorac has a relatively low risk, and that no ailin this type should be allowed to die without that the abnormality is not one which can be surgically

We wish to thank Dr J D L Reinhold for his advice about the phonocardiography, Mr D J F for the operations, Dr Martin Bodian and for necropsy and biopsy reports, Mr G H Bryant Robert for their technical assistance, and Mr D S the photographs

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# HUMAN INFECTION WITH PLEUROPNEUMONIA-LIKE ORGAN

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Although pleuropneumonia like organisms are well recognised animal pathogens, there vincing evidence that strains isolated from human disease (Nicol and Edward 1953) The animal susceptible to human strains makes pathogenicity by the application of Koch's impossible, but from the evidence set out below clear that, given suitable conditions, at least these organisms can cause severe illness

## Methods

Methods of isolation described by Edward (1 adapted for routine use

### *Media*

Since a suitable medium may be required and at short notice, it is important to use one already in use for some other purpose and is available in a fresh condition Human genital grow on defibrinated horse blood (10%) nutr after three or four days' incubation at 37 C, that the medium is fresh and remains moist strains so far found are aerobes but grow anaerobically In routine cultures growth better on the anaerobic plate because the atmo the jar is moist Aerobic plate cultures should incubated in small tins with an open tube water or sealed to prevent evaporation

Nagler's medium used for the rapid identific *Clostridium welchii* (Hayward 1941) supports of these microbes better than does blood agar improved for their isolation, without impa usefulness for other purposes, by reducing centration of agar so that the medium is sufficiently solid for handling in a petri dish P P L O are sought, the medium should be flo penicillin solution 10,000 units per ml or eryt solution 100 µg per ml., and the excess fluid tely before inoculation If thallium acetate final dilution is incorporated in the medium, the s can be isolated from discharges contaminated anisms resistant to penicillin and erythromycin medium is then unsuitable for any other purpose bs are allowed to dry before cultures are made it nely unlikely that P.P.L.O will survive The f swabs in the medium as described by Moffett 48) for the transport of gonococci has proved ccessful One strain survived on a swab in this for four days at room temperature

'Liquoid' broth method of von Haebler and 38) is suitable for the isolation of P P L O from d The blood broth cultures should be sub on both blood agar and Nagler's medium with a entration of agar *

### *tion for Growth*

es on blood agar and on Nagler's medium after ys incubation are very small only just visible ewed through a hand lens *in reflected light* ncubation does not increase their size They are nt and tend to embed themselves in the medium minute pits when they *are scraped off* This microbes and their differentiation from the of bacteria have been fully described by Edward The main difference between them and other rowing bacteria is their morphology If the are scraped from solid medium and gram in the usual way no recognisable structures will It is essential to examine them in an impression ion so that the colonies are not destroyed

ke an impression preparation, first sterilise a clean by flaming it When it is cool, press it gently on the f the medium over the suspected colonies and leave few seconds. Then lift it carefully off the medium eps, without sliding it on the surface so that the are not distorted Flame it again lightly to fix the ion and place it colonies uppermost on a glass slide the slide with paraffin wax for convenient handling by Gram's method

olonies are gram negative and have a sponge like nce with minute bacilliform and coccoid bodies at phery They are quite unlike other bacterial examined in the same way Giemsa and n stains show their structure rather better am's stain does

microbes are not easily recognisable in liquid either in stained preparations under dark illumination or by phase-contrast microscopy dium containing cells it is difficult to distinguish om the products of cell degeneration In smears ed discharges they are unrecognisable Expert handling them can be gained by culturing cervical ginal swabs from patients attending venereal clinics About 70–80% positive results can be l (Nicol and Edward 1953)

### *ic Analysis*

ccessful attempts were made to prepare aggluti antigen by centrifuging liquid cultures and by the growth from the surface of solid medium tory suspensions were sometimes obtained but ot be relied on Serological tests were therefore complement fixation only using Belyavin's modification of Fulton and Dumbell's micro o It was found that a 'chess board' titration d by Belyavin for influenza virus complement was not required because the highest con on of antigen was always the most active No s were seen

ens were prepared by centrifuging 4–5 day human (10%) broth cultures at 3000 r p m for at least one hour and resuspending the deposit from 100 ml in 4 ml of saline solution Drops of the supernatant fluid seeded on Nagler's medium yielded a semiconfluent growth and it was found that the activity of the antigen could be increased about fourfold by more efficient *centrifugation at 14 000 r p m for 30 minutes* Killing the organism by heat at 56°C rendered the suspension anticomplementary the antigen used, therefore, was an untreated living saline suspension

COMPLEMENT FIXING ANTIBODY TITRES IN HUMAN SERA (EXPRESSED AS FINAL DILUTION OF SERUM)

| Case no | *Homologous antigen* | Time after onset of symptoms | | | | |
|---|---|---|---|---|---|---|
| | | 0–10 days | From 14 days to 1 month | 1–2 mos | 2–3 mos | 6 mos |
| 1 | 1345/51 | | | 12 | 6 | < 3 |
| 2 | 8007/53 | < 3 | 480 | 120 | 12 | 3 |
| 3 | 1780*/53 | < 3 | 40 | 240 | | 21 |
| 4 | 2131/53 | < 3 | 48 | 24 | | < 3 |

Antigens for injection into rabbits for the preparation of specific antisera were also concentrated living suspensions similarly prepared but the strains were cultured in 10% rabbit-serum broth Material for the final injection was centrifuged at high speed (14 000 r p m for 30 minutes) Rabbits were injected intravenously on days 1 2 4 6 8 and 9 They received on each occasion the deposit from 90 ml of fresh 4–5 day culture A titre of complement fixing antibody of about 2880 could be expected on the 14th day It began to fall 14 days later—i e a month after the first injection The rabbits showed no sign of illness

## Clinical Records

**Case 1**—A woman aged 43 was delivered of her first child on Jan 13 1951 The delivery was difficult and performed with forceps On the second day of the puerperium, while receiving sulphonamide she developed pyrexia (103 F) Soluble penicillin 1 mega unit followed by procaine penicillin 300 000 units twice daily had no effect on the temperature which continued to swing between 99 and 103 F during two days treatment which was then discontinued

*Investigations* made on the fifth day after delivery gave the following results. Blood-cultures (in air in air plus 5–10% carbon dioxide and anaerobic) yielded a pure growth of P P L O on the tenth day of incubation Microscopy of the urine showed 8 pus cells per 1/4 inch field a culture (blood agar aerobic 1 day at 37 C) was sterile A high vaginal swab contained degenerate pus cells gram negative bacilli, and gram positive cocci and on culture (blood agar 2 days at 37 C) yielded a fairly heavy growth of *Escherichia coli* and anaerobic fusiform bacilli A white-cell count showed 13 000 per c.mm. (polymorphs 98%)

*Treatment*—On the sixth day although the blood-culture result was not yet known the patient was given aureomycin. Her temperature immediately began to fall and was normal by the end of the eighth day She was discharged fit on the twenty sixth day after an investigation for renal disease which proved negative Samples of serum were collected to be examined for antibodies against the organism isolated from her blood (see table)

The titres recorded from case 1 are low in relation to the severity of her illness but this is not surprising because when they were estimated experience had not been gained in the preparation of antigens and in the light of later work probably only a high titre serum would have reacted at all with the crude antigen then used Unfortunately when a satisfactory antigen became available the sera were unsuitable for further tests

**Case 2**—A girl, aged 1 with bronchiectasis was admitted in April 1953 for removal of the basal segments of the lower lobe of her right lung Treatment with penicillin 250 000 units six hourly was started the day before operation The day after operation the patient developed a small bronchopleural fistula, which was closed on the evening of the same day, penicillin being introduced into the wound On the sixth day her general condition was improving Her temperature had ranged between 100° and 101°F since the operation. On the seventh day a drainage tube was removed from the wound, and six hours later the patient had a rigor, and her temperature rose to 103°F and remained high and swinging for five days

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* of these methods are also to be found in my *Clinical* ology London 1955

*Investigations*—A blood count showed 14,000 white cells per c mm (polymorphs 80%) and radiographs of the chest revealed fluid in the right pleural cavity Blood cultures in air, in air plus 5–10% carbon dioxide, and anaerobic were sterile during three weeks' incubation A swab taken from the wound shortly after the rigor yielded a pure growth of P P L O Fluid aspirated from the pleural cavity five days later also yielded a pure growth of this organism, which was resistant to penicillin and sensitive to aureomycin.

*Aureomycin treatment* was followed by clinical improvement, and the temperature fell to 100°F three days later Fluid aspirated from the chest after five days' aureomycin treatment showed numerous pus cells, but the cultures were sterile On the following day a rib was resected to drain the empyema, after which the child made an uninterrupted recovery and was discharged healed nine weeks after the original operation The results of tests for P P L O antibodies on several samples of serum are seen in the table

**Case 3**—A married woman, aged 31, undergoing investigation for sterility was admitted on Sept 3, 1953, acutely ill with abdominal pain and fever She had a long history of abdominal sepsis At the age of 16 she had been in hospital for three months after appendicectomy In 1946 she was operated on for bilateral tubo ovarian abscesses The investigation for sterility had revealed a right hydrosalpinx, and twelve days before admission her fallopian tubes had been radiographed

*On admission* her temperature was 103°F, and investigations gave the following results A high vaginal swab contained numerous pus cells and mixed organisms, and on culture (blood agar 2 days at 37°C) yielded a heavy growth of anaerobic streptococci A white cell count showed 14,700 per c mm (polymorphs 77 5%) No abnormality was found in the urine

*Treatment* with penicillin and sulphonamide for two days produced no effect On the third day a second swab was cultured and streptomycin was given A high vaginal swab contained numerous pus cells but no microbes, and on culture (blood agar aerobic and anaerobic 3 days at 37°C) yielded a heavy growth of P.P L O and a scanty growth of *Esch coli* On the fourth day treatment was changed to aureomycin, after which the temperature never rose above 101°F and the patient's general condition improved On the eighth day a large right tubal abscess was aspirated per vaginam No microbes were seen in the smear of the pus, and cultures yielded a heavy growth of P.P L O and a few colonies of *Esch coli* Colpotomy was done on the ninth day and was followed by an uneventful recovery Results of serological tests are shown in the table

**Case 4**—A married woman, aged 24, was delivered of her second child on Nov 24, 1953, at home She was rescued from a severe postpartum hæmorrhage by the "flying squad" and was admitted to the hospital the same night No antibiotics were given Three days later the patient was well, apart from slight persistent pyrexia (99°–100°F)

*Investigations* gave the following results A high vaginal swab contained moderate numbers of pus cells but no microbes, and on culture (blood agar aerobic and anaerobic 3 days at 37°C) yielded a pure growth of P P.L.O No abnormality was found in the urine The fever subsided on the eleventh day of the puerperium without antibiotic treatment A second high vaginal swab, taken fifteen days after delivery, showed fairly numerous epithelial cells and a few pus cells, and on culture yielded a scanty mixed growth No P.P.L.O were isolated The results of serological tests are shown in the table

## Controls

Of 172 sera tested 171 were negative—i e, they gave titres less than 3 They comprised the following

107 sera sent for Wassermann reaction and found negative

34 from patients with acute respiratory infections (sera taken between tenth and thirty fourth days after onset and ation for virus antibodies)

1 primary atypical pneumonia, second week,
tinin and streptococcus M G agglutinin positive.

19 from women six weeks after childbirth.

5 from pregnant women

1 gonococcal arthritis (gonococcal compl
test positive)

1 arthritis (gonococcal complement fixation tes

2 Bartholin's abscess with less than a week's h

1 abdominal abscess with 2 week's history

One serum from a patient with a six days'
Bartholin's abscess and a positive gonococcal co
fixation test (titre 24) gave a P P L O titre of
abscess opened spontaneously, and the pus
cultured The patient had had a similar abs
three months previously, and the pus showed no
in the smear and on culture yielded no signific
unfortunately one of the plates was con
Selective medium for P P.L O was not used. Th
is still under investigation

Positive reactions with the sera of
uninfected patients, which were observed by
et al (1946) in their serological investigation
specific urethritis, were not seen in the presen
gation Their complement fixation method had
successful in testing the sera of cattle with c
bovine pleuropneumonia Possibly, however, t
gen was not suitable for testing human sera
although the strains used were of human
medium in which they were cultured conta
ox serum, which during extraction of the an
have given rise to some non specific substance
reacting with human serum

The strain isolated from the blood has been
by Dr D G ff Edward, who classifies it with th
type 1 genital strains (Edward 1954) The othe
appear to be culturally and serologically simil

## Bacteriology

All four strains are aerobes and showed
colonies on moist fresh defibrinated horse bl
after three days' incubation at 37°C on first
Further incubation did not increase the size of th
which dried up and finally disappeared. Th
maintained until April, 1954—i e, from four
three years—by subculture twice weekly on F
(5%), human serum or plasma (20%), and
agar † without protection by antibiotics or oth
inhibitors Their morphology and cultural
teristics remained constant, and there was no
reversion to a normal bacterial form They
maintained on a selective medium to lessen th
contamination They are all sensitive to
oxytetracycline, and chloramphenicol, moderate
tive to streptomycin, and resistant to pen
erythromycin

All four strains from these patients and th
isolated in mixed culture from the cervix o
attending the venereal disease clinic appear
serologically homologous when tested against
human sera or the specific rabbit sera High
sera inhibited their growth (Edward 1950),
effect was not seen with the comparatively
human sera

## Discussion

These four patients all showed a clinical p
infection Culture of appropriate specimen
conditions suitable for the growth of aerobic and a
pyogenic bacteria yielded a heavy growth of
and no other cause for the symptoms could b
In three of the cases recovery followed treat
aureomycin, to which the strains were sensiti

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† Nagler's medium for the identification of Cl welch
1941)

atment had failed In two cases the microbe t be isolated from the original site of infection atment with aureomycin Finally in three of ents specific antibody developed during the reached a maximal titre at about three weeks onvalescence, and fell thereafter No antibody d in sera from uninfected patients or in the sera its with other infections

is therefore good evidence that the P P L O from these patients were responsible for the symptoms It might, however be argued that ier pathogen had been killed by antibiotic treat fore the specimens were taken This does not case 4, who received no antibiotics and seems in the other cases, since there was no clinical ment until an antibiotic effective against P P L O l Primary infection by a virus could be postu ut a purulent exudate present in three of these not a feature of the virus infections so far recog Symbiotic infection with a virus cannot be but in the absence of evidence such an ion seems needlessly complex

is particularly interesting because even though tion was clinically very mild and was followed taneous recovery specific antibodies developed. was not very high but the gonococcal comple ation test often yields titres which are no higher ch are nevertheless accepted as of diagnostic ace

rological findings in the cases reported indicate complement fixation test may be useful in the ation of non specific urethritis and venereal Consistently negative results in tests of of serum obtained from patients at suitable against pathogenic human genital strains of would make it very improbable that such is were responsible for the clinical condition ion of the test does not require the maintenance cultures of the organism, for a freeze-dried ion of antigen remains suitable for at least nine

## Summary

cases of human infection with P P.L.O are d: two of puerperal sepsis one pyosalpinx and stoperative empyema Methods of preparing for serological diagnosis and for the isolation of microbes from infected discharges are briefly d

ssion preparations are essential for the micro examination of colonies

media must remain moist during three or four cubation

material examined must be fresh or taken on a d placed in transport medium

en suitable for human serological diagnosis by ent fixation is a concentrated living suspension organism

to thank Prof Wilson Smith for his encouragement re throughout this investigation, and his technical help in the preparation of antigens; Dr I M for isolating the strain from case 1 and for main he cultures for several months; Dr F F Bowers for the strain from case 4; Dr F O MacCallum for serum from cases of respiratory infection Dr Edward for examining strain 1346; and Mr J D S rof R S Pilcher and Prof W C W Nixon for on to publish their cases.

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# ŒSOPHAGEAL REFLUX

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Œsophageal reflux has received much attention from radiologists and surgeons so its incidence and clinical features are well known but the conditions under which the cardia becomes incompetent except the common association with hiatus hernia have remained obscure

In the investigation described here the intra-œsophageal and intragastric pressures were measured in an attempt to define the changes accompanying reflux and to find if any constant pattern of events precipitated reflux

## Methods

The pressures were measured through fine 'Polythene tubes with Hansen capacitance manometers (Dornhorst et al 1954) In most experiments three tubes were used together joined at the tip and recording through lateral holes usually 5 cm apart The tubes were filled with water and the distal parts beyond the recording holes were filled with mercury which enabled the exact position of the recording holes to be localised by radiography The respiratory movements were simultaneously recorded by pneumography

Twelve cases of œsophageal reflux were investigated, in four of these the cardia was in the normal position, determined by barium studies and in eight a hiatus hernia was present Twelve cases with normal function of the cardia were studied as controls

## Results

### *Recognition of Reflux from Pressure Changes*

A pressure change due to œsophageal reflux could be detected In two cases simultaneous screening of the patient after drinking a barium emulsion confirmed the relation between the pressure change and the radiological appearance of reflux Superimposed on the normal respiratory pressure-swing a positive pressure-wave about 5 mm. Hg passed very rapidly up the œsophagus (fig 1) This wave lasted 1–2 sec and was a simple peak in shape often leaving the œsophageal pressure at a slightly higher level than before until the refluxed substance was expelled from the œsophagus In this latter respect it resembled the initial rise in pressure in the œsophagus

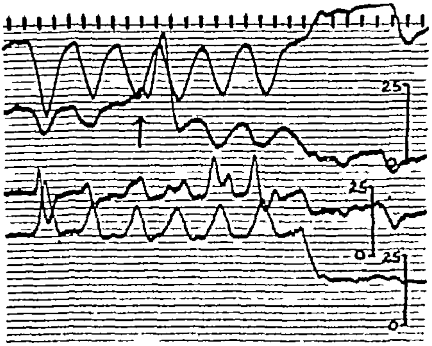


Fig 1—Recording from patient with normal position of the cardia leaning forward in bed. Top tracing: pneumogram (inspiration downwards) Lower three tracings are recordings from tubes 5 cm. apart: top tube in œsophagus; middle tube at cardia; lowest tube in stomach. Arrow indicates reflux Initiating propulsive wave At the end of the recording the patient changes position (see fig 2)

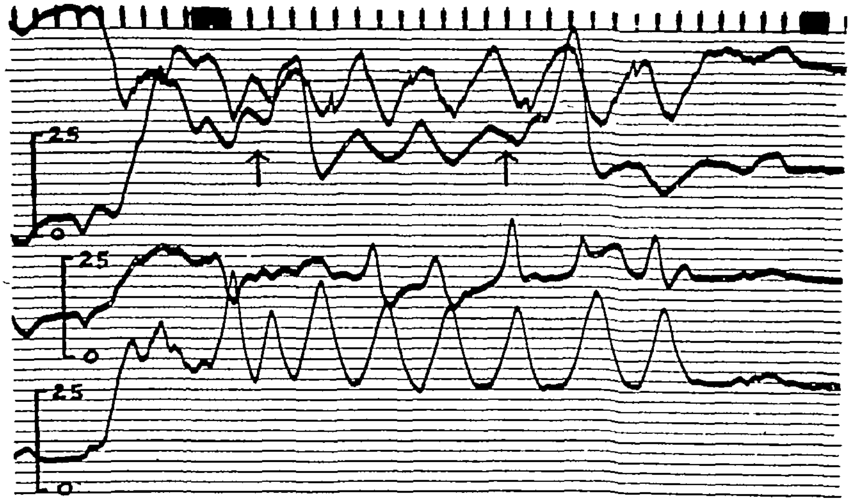


Fig 2—Recording from same patient as fig 1 leaning forward at beginning of recording Top tracing : pneumogram (inspiration downwards) Other tracings as in fig 1 Arrows indicate reflux shown in œsophageal tracing by diminished fall in pressure with inspiration followed by propulsive waves Final signal at top of record marks onset of heartburn

on swallowing Similar pressure waves were seen whether the substance refluxed was fluid or gas In cases where gas was refluxed the positive pressure wave appeared simultaneously in all parts of the œsophagus Where the substance refluxed was fluid the pressure-wave was sometimes limited to the lower œsophagus and sometimes diminished in height as it progressed upwards No general rise in intragastric pressure near the cardia preceded reflux, and the shape of the wave and the rapidity of its passage showed clearly that this was due entirely to the entry of gastric contents into the œsophagus and not to reverse peristalsis Reverse peristalsis has never been observed in any case of œsophageal reflux and only in one patient who had a postoperative stricture at the lower end of the œsophagus Instead of the positive wave there may be only a failure of the intra œsophageal pressure to drop with inspiration, but this seems to be less common (fig 2)

*Œsophageal Reaction to Reflux*

When gastric fluid appeared in the œsophagus, a propulsive wave was often initiated which progressed normally to the cardia, leaving the intra œsophageal pressure at a normal level (fig 1) This wave seemed to be caused by the presence of fluid in the œsophagus, because it could be provoked by injecting water through a tube into the œsophagus Following the pressure changes of gas reflux the pressure in all parts of the œsophagus usually rose simultaneously and eructation occurred In patients with the symptoms of œsophagitis reflux sometimes initiated uncoordinated contractions, many of which seemed to be localised and did not proceed normally cardia Œsophageal within 30 sec. after the gastric fluid into the was not related to the contractions (fig 2)

*Conditions Predisposing*

A reflux wave occur ing inspiration Further reflex was present at beginning of inspiration reflux wave rose with the increase in pressure Reflux did not every inspiration and times intermittent (fig

Reflux occurred more in some positions than was most often found patient leaning forward in bed, and after this patient supine Small the patient's posture caused reflux The

ence across the cardia was measured in by withdrawing a recording tube from the the œsophagus (fig 3) The pressure difference

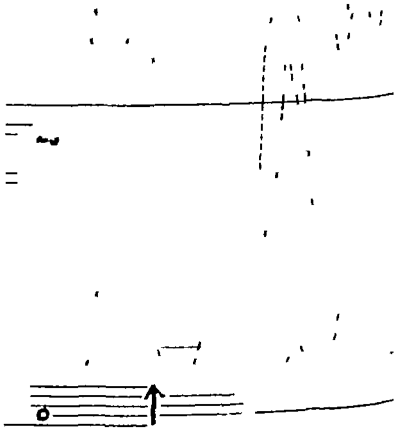


Fig 4—Recording from patient with hiatus hernia and tracing pneumogram (inspiration downwards) tracings are recordings from tubes 5 cm apart in œsophagus bottom tube in hernia. At start of changes position slightly and then reflux occurs initiates propulsive wave. Note similarity of to that of normal intragastric pressure

only 1–2 mm Hg in all positions from lying toe-touching and was about In positions, such as where the abdomen is the intragastric and intra- pressures about the together

*Pressures in Hiatus Hernia*

The observations listed collected mainly from patient the cardia was in the norm Similar results were obt patients with hiatus hern Pressure recordings from within a hernia often showed from the usual respiratory swing recorded in the œsoph common pattern was a bi

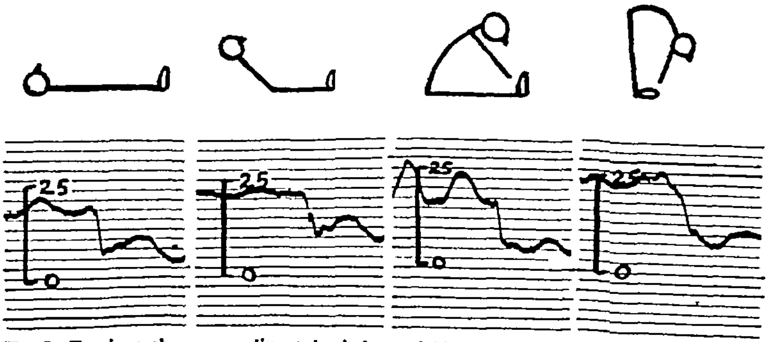


Fig 3—Tracings show recording tube being quickly withdrawn from stomach to œsophagus in different positions Note that pressure difference during expiration varies mm Hg

th inspiration (fig 5) though occasionally rn closely followed that of the intragastric swing (fig 4) It was shown in these cases cardia was not incompetent the whole time ing tube at the cardia showed with inspiration l rise of pressure followed by a fall as the ig diaphragm pulled the closed cardia over the hen the cardia was open this pattern was altered pressure did not fall

### Discussion

these observations on pressure changes the facts about œsophageal reflux become apparent

s possible to recognise reflux as a positive pressure he œsophagus and less often by a diminished drop sophageal pressure during inspiration

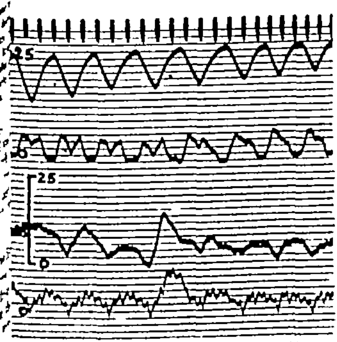
lux takes place only during inspiration

lux takes place in some positions more commonly rs, and small changes in posture may render the ompetent

se changes in posture are not accompanied by any ble change in the pressure gradient across the cardia

tructures forming the cardia are mobile and in their relative positions are easily induced by n of posture This can be seen from routine neal radiographs Probably in patients with eal reflux the competence of the cardia depends lative anatomical shape The association with on is interpreted as positional, the descending m flattening the fundus of the stomach There idence of a pressure change forcing the cardia of reverse peristalsis Dornhorst et al (1954) examining the normal cardia at operation nder it incompetent only by manipulating the o that it formed an obtuse angle with œsophagus. orkers have shown that the cardia acts as a valve ulate that it is formed by the lax gastric mucosa rea. The above mentioned observations fit well s conception because changes in the shape of ia must be reflected by changes in the tensions ucosa.

ct that reflux takes place solely with inspiration r evidence that the right crus of the diaphragm part in maintaining the competence of the cardia, its effect should be maximal during this time method of detecting œsophageal reflux may be because it is well known that reflux may be to demonstrate radiologically in cases where the diagnosis is reasonably certain.



ecording from patient with hiatus hernia. Upper tracing : gram (inspiration downwards) Lower three tracings are ges from tubes 5 cm. apart : top tube in hernia ; lower two hagus. This is reverse of positions in figs. 1 2 and 4. Note ttern of respiratory pressure-swing from hernia.

### Summary

Œsophageal reflux is accompanied by pressure changes in the intra œsophageal pressure which can be used to detect its occurrence

Reflux takes place only during inspiration and more commonly in certain positions of the patient than in others There is no appreciable change in the pressure gradient across the cardia in these positions and it is postulated that the competence of the cardia depends on its anatomical shape

No evidence was found of reverse peristalsis and the observed facts fit well with the conception of a mucosal valve guarding the cardia

I wish to thank Dr A C Dornhorst for help and encouragement during this investigation and Mr R W Halls and Mr M G Ventom for technical assistance

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# APLASTIC ANÆMIA FOLLOWING MEPACRINE TREATMENT OF LUPUS ERYTHEMATOSUS

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The earliest reference to the treatment of lupus erythematosus with mepacrine appears to be that by Popoff and Kutintscheff (1943) who recorded the successful treatment of 6 patients Page (1951) reported a series of 18 patients in many of whom the drug controlled the lesion and this form of treatment is now firmly established

The toxic effects have included blood dyscrasia Apra (1953) described leucopenia and Wilkinson (1954) agranulocytosis Vilanova and de Moragas (1953) reported 1 death from agranulocytosis Sawicky et al (1952) and Parmer and Sawitsky (1953) each noted 1 fatal case of aplastic anæmia in patients with lupus erythematosus who had been treated with mepacrine A further such case is reported here

### Case report

A woman farm worker aged 53 had had chronic discoid lupus erythematosus for some years and in 1952 she was successfully treated with mepacrine hydrochloride 100 mg t.d.s Thereafter she took intermittent courses of mepacrine in this dosage In February 1954 because of a relapse in her skin condition she again started to take mepacrine hydrochloride 100 mg t d.s. and continued until she had taken about 200 tablets (20 g ) In early May a fortnight before admission, she stopped taking the drug and then noticed two large bruises which had appeared without apparent preceding trauma. Thereafter bruises appeared at short intervals, and later purpuric spots, especially on the legs followed by melæna and hæmatemesis. Her consumption of foods containing ascorbic acid had been low and her doctor had prescribed tab ascorbic acid 50 mg t d.s on the day before admission There was no family history of a bleeding diathesis.

*Examination* —The patch of lupus erythematosus was scarcely discernible as a faintly pigmented area on the left cheek. The skin of the face forearms and legs was conspicuously yellow There were numerous petechiæ on the trunk and limbs together with many ecchymoses of varying age and size some as large as 2 in. in diameter No enlargement of lymph glands was found Systematic examination showed no other relevant abnormality

*Investigations*—Urine, normal  Blood  Hb 64% (Haldane), red cells 3,150,000 per c.mm, white cells 1900 per c mm (neutrophils 24%, lymphocytes 76%), platelets 70,000 per c.mm, clotting-time 7 min, bleeding time over 80 min, Hess test positive, erythrocyte sedimentation rate 118 mm in 1st hr (modified Westergren)  Serum bilirubin 0 5 mg per 100 ml  Plasma proteins 5 7 g per 100 ml (albumin 4 2, globulin 1 5)  Cephalin cholesterol flocculation test negative  Alkaline phosphatase 9 King Armstrong units  Prothrombin concentration 100%  Ascorbic acid saturation test (700 mg given daily by mouth) urinary output 11 mg on 1st day and 66 mg on 2nd day

*Progress*—On the day after admission, blood examination showed Hb 29% (alkaline hæmatin) (4 4 g per 100 ml), red cells 1,380,000 per c mm, packed cell volume 13%, mean corpuscular volume 94 c µ, mean corpuscular hæmoglobin concentration 34%, white cells 2600 per c.mm (neutrophils 29%, lymphocytes 70 5%, monocytes 0 5%), platelets 25,000 per c mm, bleeding time over 60 min, coagulation time (capillary tube) 2½ min  Sternal puncture showed a few scattered, damaged marrow cells, on which a definite opinion could not be passed

After transfusion of three bottles of blood (approximately 1500 ml) the hæmoglobin was 42% (Haldane)  The patient then became febrile, and despite treatment with penicillin and later erythromycin her condition deteriorated  Bullæ appeared on the trunk, and the hæmatological findings remained virtually unchanged  A course of corticotrophin (Armour) 80 units daily was given for 4 days, but she died in coma on the 11th day in hospital  Blood for culture taken 2 days before death proved sterile

*Necropsy*—The examination was made 19 hours after death  Advanced putrefactive changes were present, with swelling of the face, neck, and abdomen  The superficial veins were outlined in a dark red colour  The subcutaneous tissues were crepitant, and rigor mortis had passed off  Diffuse petechial hæmorrhages and ecchymoses were present with areas of superficial desquamation some ulcerated  Internally, the only distinct lesions were petechial hæmorrhages in the subepicardial fat and throughout the mucosa of the whole intestinal tract  The marrow of the mid shaft of the femur showed no evidence of reactive hyperplasia

Microscopically, all organs had been invaded by *Clostridium welchii*  Sections from the bullous areas showed a superficial line of separation in the epidermis, in or just below the keratin layer  No polymorph reaction was present in the blister fluid or deeper layers, and no inflammatory reaction at the buttock ulcer—a former injection site  There were no changes suggesting lupus erythematosus in the renal glomeruli

Bone marrow (vertebral) showed a few small scattered foci of hæmopoietic cells, which, owing to putrefactive changes, could not be identified  The appearance was consistent with marrow aplasia

### Discussion

Custer (1946) found 57 fatal cases of aplastic anæmia among Servicemen in the South-West Pacific theatre, where the vast majority took suppressive doses of mepacrine (100 mg daily)  In other war theatres the incidence of aplastic anæmia in the Services was, by comparison, insignificant

Fishman and Kinsman (1949) described 7 military patients who had been on suppressive treatment with mepacrine and developed hypoplastic anæmia, 3 of these eventually died  Bruce Chwatt and Bruce Chwatt (1950) and Riesgo (1951) reported similar fatal cases

It would seem well to bear in mind the possibility of bone marrow damage in patients treated with mepacrine  Although agranulocytosis can occur without warning, by regular blood counts impending marrow aplasia might sometimes be recognised before irreparable damage had occurred  That this is possible is suggested by the experience of Fishman and Kinsman (1949)  Of their seven patients, four recovered

### Summary

Fatal aplastic anæmia is reported in a patient with localised lupus erythematosus who had been treated with mepacrine

The risk of marrow aplasia resulting from administration of mepacrine should be rem treating patients with lupus erythematosus

We are grateful to Dr J M Drennan for the p report

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# MALIGNANT SENSORY NEUROP

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It has been recognised for many years that disturbances are occasionally associated disease in the absence of any obvious meta ment of nervous tissues  Recorded cases, comparatively few, suffice to show that a of unusual neurological disorders accomp with a significant frequency" (Henson et Among these disorders subacute cortical degeneration (Brain et al 1951), proximal pathy (Hart 1954), and sensory Brown 1948) are separable as fairly distinct other less well defined clinicopathological from lesions involving virtually any part of and peripheral nervous systems and also m myopathy, mixed types of polyneuritis peripheral and cranial nerves, pyramidal and mental changes occur sometimes in almost but more often in varying combinations. H (1954) recently described five cases of cerebell six of neuropathy, and eight of myopathy, and and Williams (1954) two cases of sensory ne one of motor neuropathy, and one of myopath two reports demonstrate the diversity of ne disorders that may be associated with c Furthermore, purpuric states, venous throm baum and Strich 1953, Williams 1954), and carc emboli (Smith and Whitfield 1954) are ciated with carcinoma and may result in lesions responsible for the presenting clinical

Instances in which peripheral neuritis of dominantly sensory type was associated with carcinoma have been described by Parke Hill (1933), Denny Brown (1948), Wyburn Ma Kremer and Pratt (1952), Heathfield and Willi and Henson et al (1954), while Dodgson and (1953) recorded a case in which the primary gr œsophageal

The neuropathy has usually been gross and striking feature  Necropsy has shown demye the posterior columns and posterior nerve roots, tion of nerve cells in the posterior root gangli development of cellular nodules resembling the nodules of Nageotte" (Nageotte 1907), nerve degeneration, and some muscle atrophy

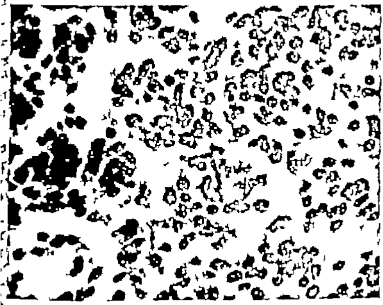
Gross neuropathy of wholly sensory type found, and there can be no doubt that in the diabetes and alcoholism malignant disea o be present, even though at first it may not to detect. A striking example of this type is below

## Case-report

ied woman aged 66 was first seen on June 16 195_ always been of nervous temperament but otherwise healthy until February 1952 She then developed of burning and smarting all over her abdomen and h legs. Her legs felt wooden and she could not walk her arms felt cold, and her fingers numb and weak weeks before she was first seen she had sustained a urn of the right foot which appeared to be [illegible] com ry strikingly little pain. Her consumption of alcohol at life had been negligible

*ation.*—The patient's gait was very ataxic and there of sense of position and of sensibility to deep pain rick over the legs and feet while the hands showed ensibility to vibration and pinprick The ankle right biceps jerk, and both triceps jerks were absent s no motor loss or wasting The hæmoglobin was there was no glycosuria the chest radiograph was d no abnormality could be detected in the abdomen

—The patient was treated with vitamin B complex ew of her failure to improve she was admitted to the lizabeth Hospital Birmingham, on Dec 27 1952 A efore admission she had sustained a further deep but burn of the right knee from sitting in front of the ere was still no motor loss or wasting in the limbs but ory polyneuritis was much more severe The gait was ataxic all the tendon jerks were absent in upper and limbs and there was pronounced impairment of all f sensation in the hands and forearms and the whole ower limbs Even over the trunk sensory acuity was at diminished. A blood-count was normal and a tal test meal showed abundant free acid The cerebro luid (C.S.F.) which was under normal pressure showed ormality on cytological and chemical examination. assermann reaction was negative in blood and C.S.F. e urine did not contain lead porphyrins, or arsenic tient had obviously lost a great deal of weight and so a search for malignant disease was again instituted A adiograph showed no abnormality; the breasts and were normal; radiography after a barium meal no abnormality in the alimentary tract nothing tal was found in the urine; and the fæces were negative ult blood A complaint of previous vaginal bleeding estigated by a gynæcologist Dilatation and curettage senile endometritis but no evidence of a pelvic m.



Anaplastic small-cell carcinoma of bronchus. (Hæmatoxylin and eosin.)

e patient's husband was dying of a pancreatic neoplasm t hospital after a month and was not seen again until 1953 She was then so ataxic that she could scarcely or walk Motor power in the upper and lower limbs d good; but all tendon jerks and the plantar responses bsent all forms of sensation were totally lost below guinal ligaments, and perception of pinprick and light were grossly impaired in the forearms and hands,

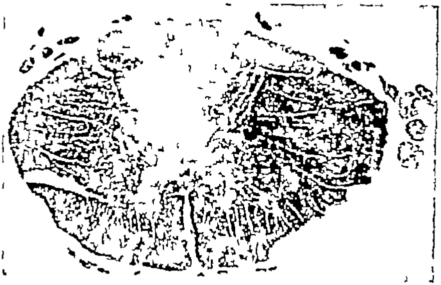


Fig 2—Cervical cord showing demyelination of posterior columns and posterior roots. The nick marks the right anterolateral column (Frozen section Weil's myelin method.)

particularly the left Blisters were present on both heels. Cough and sputum had been troubling the patient for two or three weeks and a large right pleural effusion was present which on aspiration was found to be bloodstained Radiography of the chest showed a mass in the right lower hilar area, and radiography with a barium swallow showed indentation of the œsophagus at the level of the tracheal bifurcation and again two inches below Auricular fibrillation was present. The patient's general condition was very poor and she became progressively more dyspnœic and died one week after admission eighteen months after the onset of neuritic symptoms.

*Necropsy*

A large carcinoma of the right lower lobe bronchus was infiltrating the lung substance and extending proximally along the bronchus towards the tracheal bifurcation There was a right pleural effusion of about three pints and a large mass of hilar lymph nodes containing secondary deposits was displacing the œsophagus anteriorly and infiltrating the posterior surface of the heart No other metastases were found on naked-eye examination anywhere in the body Ante-mortem thrombus was found in the ascending aorta and was adherent to the aortic valve The brain and spinal cord showed no significant naked-eye changes.

*Histologically* the bronchial growth was an anaplastic carcinoma composed of small darkly staining round and oval cells (fig 1) an oat-cell type of structure was seen in many areas Sections of lung remote from the carcinoma showed no infiltration. The hilar lymph nodes were extensively infiltrated with secondary growth, as was the whole thickness of the left auricular myocardium, carcinoma cells being present on the endocardial surface Partly necrotic cellular tissue resembling degenerating carcinoma was seen in the centre of the aortic thrombus, but no unequivocal non degenerate carcinoma was present Apart from interstitial

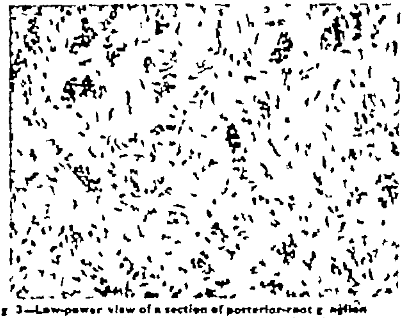


Fig 3—Low-power view of a section of posterior-root g [illegible] loss of neurones and numerous "residual nodules." [illegible] and eosin.)

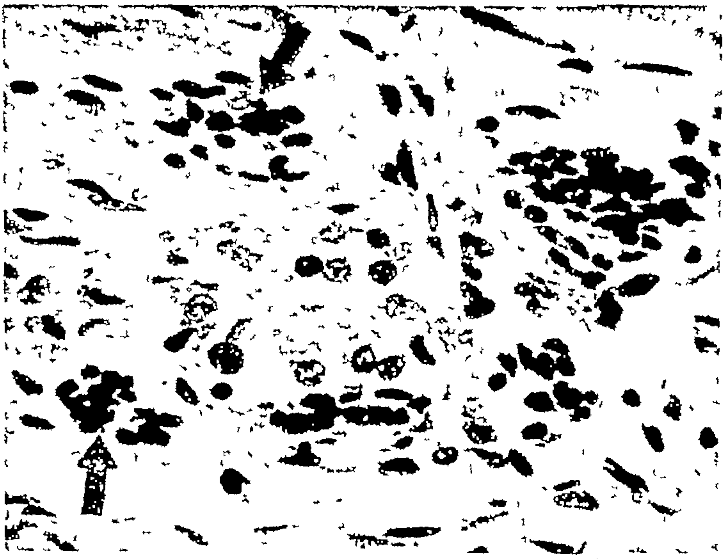


Fig 4—High-power view of posterior-root ganglion showing three adjacent "residual nodules" (arrowed) arranged around a degenerate ganglion cell which is in the centre of the field Note the smaller clusters of dark cells just below this degenerate ganglion cell (Hæmatoxylin and eosin)

fibrosis of the thyroid no other significant changes were seen in any other viscera, including the endocrine organs The bone marrow was normal

The spinal cord showed demyelination of the posterior columns with slight gliosis (fig 2) The posterior roots were demyelinated, but the anterior roots, anterior horns, and anterior and lateral columns, all appeared normal The posterior root ganglia showed a great reduction in the number of ganglion cells and numerous clumps of small cells with darkly staining round or oval nuclei and only a small amount of cytoplasm, some of these cellular clumps were ringed by larger, paler, capsular cells These resembled the "residual nodules of Nageotte" which are said to develop as a result of changes in the periganglionic satellite cells, after degeneration of ganglion cells which have disappeared by the time the nodules are fully developed (figs 3 and 4) Lipo fuscin pigment was demonstrated in relation to some of the nodules and in the few surviving ganglion cells by the periodic acid Schiff stain There was patchy wallerian degeneration of the peripheral nerves, and sections from the leg, lumbar, shoulder, and intercostal muscles showed non specific atrophic changes The only other changes in the nervous system consisted of occasional foci of small darkly staining cells in the cerebral perivascular spaces, subarachnoid space, posterior roots and ganglia, and the epidural fat around these ganglia Some of these cells were lymphocytes, but others were atypical and possibly carcinoma cells

## Discussion

The histological features in this case accord very closely with the descriptions of Denny-Brown (1948), Heathfield and Williams (1954), and Henson et al (1954), and the clinical features of all recorded cases have been almost identical It appears that there is a dominantly or wholly sensory neuropathy of distinctive character, resulting from changes in the posterior-root ganglia, posterior roots, and posterior columns, which occurs in association with carcinoma The carcinoma has always been bronchiogenic except in the case described by Dodgson and Hoffman (1953), in which the primary neoplasm was a squamous carcinoma of œsophagus In this case the only available fragment of posterior root ganglion did not show typical "residual nodules" Pathological evidence of sensory neuropathy secondary to degeneration of posterior root ganglia and unassociated with carcinoma has not so far been recorded, although McAlpine and Page (1951) suggested that this can occur

The association between the carcinoma and the neuropathy has given rise to much speculation Denny-Brown (1948) [illegible] attention to the similarity of the histological changes in deficiency of pantot vitamin E in animals, and sug bronchial carcinoma may possibly by-product interfering with the pantothenic acid So far no im been claimed from vitamin therapy suggested that the neoplasm and the may have a common cause, but kno gens are generally so different poisons and act at such different rat nature of such a common cause is conceive (*Lancet* 1954)

Since this form of sensory neurop commonly associated with malignant possibility that it *may* be due to deposits of unusual type has to be Extrathoracic metastases visible on examination are not usually absence of extrathoracic spread was in our case, especially as the growth trated the myocardium and by re endocardial surface of the left auricle access to the general circulation In some factor may prevent the deve typical metastases, and therein may l to the problem Three cases of "c metastatic carcinoma" secondary to genic carcinoma have been recorded ( Alpers 1951) in which macroscopically no were found in the central nervous sy microscopy showed clusters of carcinoma ce perivascular spaces and lying free in the sub the cerebral hemispheres, brain stem, cerebel spinal cord

Because in our case the cells of the "residual found in the posterior-root ganglia and the ce primary carcinoma were morphologically possibility that the nodules contained carcin has been considered (figs 1 and 4) Since, there is no consistently reliable histological m demonstrating isolated clumps of carcinoma possibility that the "residual nodules" in th root ganglia contained carcinoma cells is still Even if carcinoma cells were present it is explain how they could spread from the lun posterior root ganglia and become arranged as at the site of the nerve-cells Provided that could reach the subarachnoid space it would p possible for them to penetrate into the post ganglia in the way described for particulate m Brierley (1950), who showed that an india ink injected into the cisterna magna of rabbits foun into the posterior root ganglia where it had neuronal distribution, outlining the nerve-cells also been shown that india ink injected into th subarachnoid space of the rabbit will find its w lymph-nodes on the posterior thoracic and a walls (Field and Brierley 1948, Woollam an 1953) These experiments suggest a possible ro which carcinoma cells may spread from the l lymph nodes to the posterior root ganglia

Whatever may be the basic cause of the ne lesions, it seems that the demyelination of columns, dorsal roots, and peripheral nerve re secondary degeneration of the central and p processes of atrophic posterior root gangl Denny-Brown (1948) concluded that the muscle in his cases were due to primary muscle de ("polymyositis"), but in our case the atroph showed no specific histological changes Mea practical point is that a carcinoma has been pre pathologically substantiated cases of this dist of sensory neuropathy, and at the time the ne develops the growth may be occult

## Summary

clinicopathological features of a case of wholly
neuropathy associated with bronchial carcinoma
cribed

neuropathy may possibly result from an unusual
f carcinomatous infiltration of the dorsal root

are indebted to Prof J W Orr Dr Michael
n and Dr A. D B Mackie (the patient's own doctor)
ir help in the investigation and management of this
Part of the histological examination was made possible
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ham Hospitals

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# Preliminary Communications

## MMEDIATE EFFECTS OF THYROXINE ANALOGUES ON BIOLOGICAL OXIDATIONS IN VITRO

E the elucidation of the structure of thyroxine
ain lines of inquiry have been followed in this
y the thyroid physiologist and biochemist the
of the circulating thyroid hormone, and the form
h it is active in the peripheral tissues The former
o problems has now been resolved but not the
The latent period of action of thyroxine and
compounds in vivo and in vitro has been a puzzle
search has been made for a derivative of thyroxine
might produce a rapid thyroid like effect

acetic acid analogues of thyroxine and triiodo
ine have been shown to possess activities similar to
f thyroxine in goitre-prevention assay in rats[1] the
acetic acid also raises the metabolic rate of intact
hen given in repeated doses,[1] and gives thyroxine
ment effects in thyroidectomised birds[2] It was
re thought of interest to study the action of these
unds on an in vitro system

ault[3] has observed that neither thyroxine nor
thyronine exerts an immediate effect on the
tion of rat-kidney slices in tyrode buffer but that
prolonged incubation period (3 days) at 4°C an
iable rise in oxygen consumption can be seen
resent communication deals with the effects of the
cid analogues of thyroxine and triiodothyronine
system

### METHODS AND RESULTS

ney slices from thyroidectomised rats which had
fasted for 24 hours were incubated in tyrode
n in the presence of the two test compounds and
trol solutions and their oxygen consumption was
red at short intervals by the conventional Warburg
d The results are shown in the accompanying
It will be seen that both compounds produce

PERCENTAGE INCREASES IN $O_2$ CONSUMPTION OF RAT KIDNEY SLICES

| Time (min.) | Tetraiodothyroacetic acid ($5 \times 10^{-}$ ) | Triiodothyroacetic acid ($1 \times 10^{-6}$) |
|---|---|---|
| 15 | 83 | 91 |
| 30 | 54 | 68 |
| 60 | 45 | 56 |
| 90 | 16 | 35 |
| 15 | 69 | 196 |
| 30 | 44 | 106 |
| 60 | 20 | 48 |
| 90 | 15 | [illegible] |
| 15 | 70 | 63 |
| 30 | 54 | 40 |
| 60 | 35 | 10 |
| 90 | 13 | 0 |
| 15 | 71 | 74 |
| 30 | 31 | 40 |
| 60 | 20 | 6 |
| 90 | 8 | 0 |

Each figure represents the mean of two experimental values

their maximum effect at the earliest time interval —15 minutes—and that after 90 minutes the effect had disappeared It has also been found (figures to be published later) that higher concentrations of both compounds may be ineffective or may even inhibit respiration in kidney slices. Both compounds are active at dilutions lower than those quoted, and concentrations of triiodothyroacetic acid as low as $1 \times 10^{-7}$ produce a noticeable effect At all effective concentrations both compounds exert their action without any latent period of action

### DISCUSSION

It appears that the acetic acid analogues of thyroxine and triiodothyronine are effective in raising the oxygen consumption of rat kidney slices in vitro without any latent period of action Neither of the circulating thyroid hormones—thyroxine and triiodothyronine—has any effect on this system without a pre incubation period This leads us to suggest that these acetic acid derivatives may indeed be the forms in which the thyroid hormones act in the tissues

In preliminary experiments, one of us (O T ) has found that a single dose of tetraiodothyroacetic acid 2 mg per kg body weight raises the basal metabolic rate (B.M.R ) of thyroidectomised rats (3 animals) within 0–2 hours, and that the effect wears off after 4 hours. In the whole animal therefore this thyroid like action is very much more rapid than that of thyroxine or triiodothyronine A higher dose (4 mg per kg body weight) did not raise the B M R of thyroidectomised rats this lack of action is comparable with the lack of effect of higher doses of the acetic acid analogues in vitro It would appear from these and from other reported findings that there is a threshold dose for thyroidal stimulation of respiration above which only toxic or inhibitory effects are obtained.

The immediate effects of these acetic acid derivatives on respiration in vitro are worth considering in relation to another system, studied by Thibault and her colleagues.[4,5] These workers have found that thyroxine and triiodothyronine can enhance the sensitisation of isolated intestinal muscle to adrenaline only after a short incubation period but that thyroxamine and triiodothyronamine exert this effect without any latent period of action It is not yet known whether the acetic acids or the amines derived from the circulating thyroid hormones occur in the tissues Experiments are now in progress to elucidate these questions

### SUMMARY

The acetic acid analogues of thyroxine and triiodothyronine have been shown to raise the oxygen con

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sumption of rat kidney slices in vitro without any latent period of action

We wish to thank Sir Charles Harington, D.SC., F.R.S., and Mademoiselle E Le Breton for their interest and encouragement

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PH D Lond F.R S

## METABOLIC ABNORMALITIES IN HYPOPHOSPHATASIA

IN 1948 Rathbun[1] reported from this hospital a metabolic disorder which he designated "hypophosphatasia" His report concerned an infant in whom there was defective calcification of bone matrix, associated with levels of serum alkaline phosphatase considerably below the normal range Since his original description three additional articles[2–4] and two new names ("rickets with deficiency of alkaline phosphatase activity," and "osteodysmetamorphosis fœtalis") have been added to the literature These contributions have helped to establish the clinical features of the condition

We are currently studying a female infant who developed a bulging anterior fontanelle at 3 months of age and who manifests the typical abnormalities in the skull, long bones, and serum

The fundamental disturbance in hypophosphatasia remains a matter of conjecture We record here two hitherto unreported observations which may prove helpful in elucidating the pathogenesis of the syndrome

It has been shown previously that serum from a patient with this condition does not inhibit the alkaline-phosphatase activity of normal serum We have confirmed this and have shown in addition that serum from our patient will produce in-vitro calcification in the cartilage of rachitic rats We present this as further evidence that defective calcification in hypophosphatasia results from a primary disturbance in the metabolism of bone matrix

The association in our patient of metabolic bone disease and mild renal insufficiency prompted us to study the urinary amino-acid pattern by paper partition chromatography as described by C E Dent In addition to the usual amino acids we have repeatedly found a ninhydrin positive substance similar in every property so far tested to aminoethyl phosphoric ester ($NH_2$-$CH_2$-$CH_2$-O-PO(OH)2) The material is also present in the plasma of our patient, and thus is unlikely to be a product of abnormal renal metabolism We have learned from McCance and from Dent[5] that they too have found this material in the urine of an infant with hypophosphatasia Their finding was made independently of ours and at about the same time

The substance cannot be detected in the plasma of normal persons or in urine Therefore we are now attempting to establish its identity If it proves to be aminoethyl phosphoric ester, one might speculate on the possible relation of alkaline phosphatase and the above mentioned phosphate ester in bone formation

On the basis of studies of the activity of serum alkaline phosphatase in parents and siblings, other workers have suggested that hypophosphatasia is genetically determined We have found low concentrations of the same abnormal ninhydrin-positive substance in the urine This finding further supports the sugge hereditary factors operate in the ætiology of phatasia

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D Fr
M.D To
E R T
M.D To

The Research Institute Hospital for Sick Children, Toronto, Canada

F H E C
B.Sc. M

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# New Inventions

## SANDAL OF VARIABLE HEIGHT FOR A LIMB-LENGTH DISCREPANCIES

LIMB-LENGTH discrepancies are measurable in practice with a tape-measure and, if the p by putting the foot of the shorter leg on to wood of varying heights This latter method is the one when ordering raises to the shoe or when surgical boots which contain an inbuilt raise.

The main drawbacks of this technique are patient's inability to walk with the suggested position and the considerable discomfort of their body-weight on blocks when the raises are different for forefoot and hindfoot. Because disadvantages the patient's opinion about the height is often inaccurate, and perhaps an surgical shoe made to a prescription obtain testing with blocks has to be altered later, when in the flexible shoe enables the patient's opin more accurate

To overcome these difficulties a wearable pliab has been devised which incorporates a raise of variable from $^3/_4$ in to 2 in and of the sole fr to 1 in

The basic sandal can be made for adults and For adults a length of 10 in can be used for e

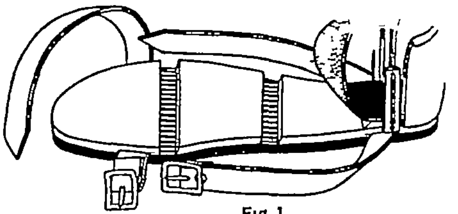
Fig 1

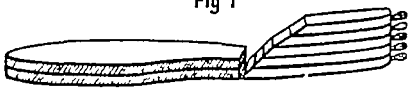
Fig 2

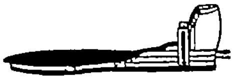
Fig 3

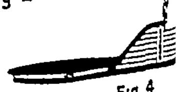
Fig 4

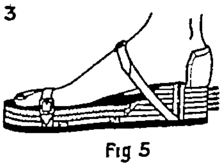
Fig 5

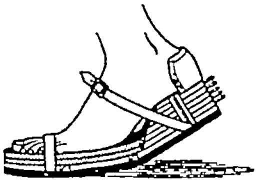
Fig 6

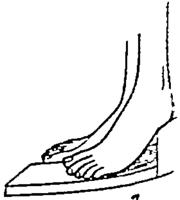
Fig 7

here is no toe-cap, a foot longer or shorter than
dal can be accommodated The design is shown
, where the sole is seen to be composed of three
of five-ply wood $^1/_4$ in thick which are connected
ece of rubber nailed under them which is $^1/_4$ in
nd shaped to serve for either foot Rubber used
-tiling is satisfactory Leather straps pass between
piece and the rubber and between the heel piece
rubber ; these should be recessed into the wood
a flat tread

he heel two aluminium slotted bars are screwed
eel piece to stand vertically at its inner and outer
they are connected by a cross piece of aluminium
like the leather straps, passes across the sandal
the five ply and the rubber Fitting in the
of the slot and able to move up to any desired
is a small heel piece of three-ply on to the top of
s stuck a thin leather insole The combined thick
these is $^1/_4$ in ; the insole is flimsy its thickness
gible, and it presents a smooth surface to the sole
oot no matter what raise is used. To the circum
of this piece of three-ply is attached a sturdy
taken from an old shoe Just in front of the edges
eel-cap small screws are inserted into the three-ply
le it to travel freely up and down in the slots of
l piece. This is the basic sandal.

varying the heel height five separate platforms of
of gradually decreasing length but of the same
and height as the five-ply of the heel piece are
g 2) Each of these has a small hook at the back for easy withdrawal or insertion These are not in any way connected to the sandal proper They lie in the desired position between the aluminium uprights and can be slid in and out easily from the back of the sandal (figs 3 and 4)

For raising the sole five-ply is not used, because this would be rigid Instead floor rubber $^1/_4$ in thick is used Fig 5 shows two pieces laid between the flimsy insole and the segmented sole ; the strap at the front plus body weight keeps them in position The fixed sandal, complete with $1^1/_4$ in heel and $^1/_2$ in sole raise, is shown both during resting (fig 5) and during walking (fig 6) Compare the awkwardness shown in equalising a discrepancy with blocks (fig 7)

The height of the sandal without additional blocks—i.e. as shown in fig 1—is heel $^3/_4$ in., sole $^1/_2$ in By measuring the height of the heel and sole of the shoe the patient is wearing on the normal leg the necessary raise can be assessed accurately

Without taking the sandal off one can quickly alter the raise on the heel by sliding in or withdrawing a further block , and, since each is exactly $^1/_4$ in. in height, a high degree of accuracy can be achieved and with it a high degree of comfort and economy

My thanks are due to Mr W Sayle-Creer for valuable help with the text and to Miss Joan Taylor, of the department of medical illustration Manchester Royal Infirmary for the drawings.

Salford Royal Hospital,
Lancs

N J BLOCKEY
M.CH ORTH Lpool F.R C.S

# Reviews of Books

## oots of Crime

tor : the late Sir NORWOOD EAST M D., F.R.C.P
merly lecturer on forensic psychiatry Institute of
chiatry Maudsley Hospital London London :
tterworth 1954 Pp 181 30s

DES papers by the late Sir Norwood East, who
pioneer in seeking to introduce psychological
s into the public treatment of crime, this book
s contributions by three psychiatrists, a probation
and a Metropolitan police magistrate. As might
ected, quality and scope are diverse and it is
determine precisely at whom the book is directed
t is the educated layman The opening chapter
Norwood, on legal and medical advances in
logy is an interesting historical survey of the
of the subject Dr John Mackwood has had
icult task of discussing remedial and educational
therapy during penal detention and he makes a
and not unsuccessful attempt to explain what
-analysis can do, even in the least promising of
ironmental circumstances. Dr Desmond Curran s
iatric approach to the offender is restricted in
says almost nothing of concepts of dynamic
logy He writes :

> sensible view must be that many individuals present
> ather than medical problems as in the case of the
> y On the information available to me this also
> or the vast majority of criminals and this remark
> d by Mr Frank Powell who writes in the concluding
> : About 80% of arrested offenders present social
> han purely medical problems

t nowadays possible to draw so sharp a distinction
n the social and the purely medical aspects
an behaviour ? If psychiatrists are to make any
contribution in this field surely work-shyness and
l behaviour of mainly social origin must be
ly studied In discussing why psychiatric evidence
ot carry more weight in courts of law Dr Curran
eter Scott and Mr Powell put all the blame on
(bad) psychiatrists who make fantastic claims.
might surely have mentioned that lawyers are as
as other mortals to unconscious resistances
Scott in dealing with the phenomena of criminal
our and the efficacy of punishment writes

> ry animal trainer uses punishment even if he is only
> strating his disapproval but he knows full well that
> get nowhere with a frightened or angry animal ; he
> must restore a friendly relationship after the punishment
> punishment of a child is never complete until he once more
> feels approved of Yet [in relation to crime] punishment
> is expected to act unaided.

One might go further and say that punishment will never succeed unless it is applied in the context of an enduring relation between the punisher (or what he represents) and the punished It is the establishment and maintenance of this relation that constitutes the most difficult aspect of the problem of recidivism Mr W Clifford writing on the rôle of probation in the treatment of offenders has concentrated much useful factual information, and has commendably eschewed controversial opinion Mr Frank Powell on the magistrate and the psychiatrist, is stimulating but incautious. His picture of the struggle between good and evil in the heart of every man calls to mind the old Negro spiritual

> In my heart there s a good man living and a bad man too
> They both try to tell me what to do

So far, so good but the song continues :

> Bad man says " You must do what isn't right ",
> And the good-a man the bad-a man they struggle in my heart
> and keep me awake all night

This, surely, is where psychiatry should come in—before the bad a man has won and there is nothing left to do but discuss whether he owes his victory to social or purely medical causes.

## Mechanism of Labour

ERIK RYDBERG M.D., professor of obstetrics and gynæcology University of Copenhagen. Springfield Ill Charles C Thomas. Oxford : Blackwell Scientific Publications 1954. Pp 180 34s

SINCE 1935 students of obstetrics have been familiar with Professor Rydberg s ideas on the mechanism of labour and with his elegant and simple models which illustrate the passage of the fœtus through the curved birth canal Here he discusses in much greater detail his hypothesis that the movements of the fœtal head during labour are determined essentially by the shape of the head and the shape elasticity and plasticity of the soft birth canal '

His argument is supported by well reproduced radiographs and by a series of experiments on necropsy specimens and on carefully prepared models Professor Rydberg discusses not only his own conclusions but also the ideas of others who offer advanced mechanical explanations of the distribution of force on the fœtal head and the derivation of the mechanical couples which produce rotation or flexion. A final chapter present subject in mathematical form, and analyses the ways in an object as asymmetrical as a skull can translate and rotate within the narrow confines of the birth canal Being mainly an account of what happens during normal vertex presentations, the book throws little light on what can be done when all is not normal Professor Rydberg implies that the shape of pelvis and head, at the outset, determines the shape of things to come, and that subsequent moulding and development of the caput make any attempt to modify the pathway difficult and often undesirable

The argument is well supported by evidence, but the author has not measured his torques and forces with internal gauges We may yet come to a fuller understanding of this subject

### Renal Function

*Transactions of the Fifth Conference, October, 1953, Princeton, N J* Editor STANLEY E BRADLEY, M D, associate professor of medicine, Columbia University, New York New York Josiah Macy, jun, Foundation 1954 Pp 218 $3 75

IN this conference nineteen American and one British expert participated Papers were given by Luetscher, Miller, and Bull, and were followed by vigorous discussion The value of these books is somewhat diminished by the long interval elapsing before publication, and the material of the first chapter has already appeared elsewhere

Speakers on the nephrotic syndrome dealt with the presence of aldosterone in nephrotic urine and with treatment by corticotrophin and cortisone Experience was reported of homologous kidney transplants in man survival of these transplants was considerably longer than in the dog, even though prolonged complete ischæmia of the transplanted organ was often unavoidable Results, however, gave little hope of permanent survival of the transplant, except possibly from an identical twin Present views of the cause and treatment of acute renal failure were discussed, and speakers described modern modifications of treatment, such as the reduction of fluid intake to as little as 800 ml each day, reliance on carbohydrate alone if oral feeding is used, and the increasing popularity of intravenous feeding by infusion of hypertonic glucose solutions into the superior or inferior vena cava

The book will be of interest to clinicians concerned with the applied physiology of renal disease, and it draws attention to the present intense research activity in this field

### Techniques de réanimation médicale et de contrôle de l'équilibre humoral en médecine d'urgence

J HAMBURGER, G RICHET, and J CROSNIER Paris Flammarion 1954 Pp 368 Fr 2600

THIS is an unusual book, and correspondingly difficult to judge The underlying thesis is that many quite different diseases are associated with failure of one or more of the regulating mechanisms by which the healthy body maintains its normality, and that we now know enough of homœostasis to enable us to maintain artificially some of these mechanisms until the natural process has been restored

The type of mechanism which the authors have in mind is shown by the subjects of successive chapters the control of respiration, water balance, electrolyte balance, excretion, the blood, and the circulation There is also a chapter on the nutrition of the acutely ill patient, and an appendix containing detailed technical methods The authors believe this to be the first book of its kind, and contend that some things can be excused in a pioneer venture which might be culpable in a textbook of the usual type On reading through some of their statements they were displeased, they say, to find that they had distorted their views by over simplifying them Medical authors, if not readers, will sympathise with them in this experience

Their underlying idea may well be sound and their claim that the techniques described are often life saving is borne out by experience The presentation is much systematised, perhaps beyond Nature, but the principles expressed seem well established There is a fair amount of padding, especially in the illustrations (e g, a drawing of how to make a blood film and a drawing of Tallquist's papers in black and white) On t[illegible] hand, hardly anything has been omitted—though there is no reference to the B L B mask in on oxygen administration which devotes a page (w illustrations) to the nasal catheter Much exper thought are reflected in this compilation and there is architect's design for a future "centre of resuscita

Perhaps the chief value of the book is that it together useful information which must sought in a whole series of special monographs

### Surgical Technigrams

F M AL AKL, M D, associate attending surgeon County Hospital, New York New York and l McGraw Hill 1954 Pp 346 96s

THIS book is made up of a series of line drawings accompanied by a short explanation, of the stages of 36 operations commonly undertaken general surgeon To describe them, the auth coined the word technigrams

Each stage of each operation is clearly shown, there are many drawings for each procedure no less illustrate radical cure of an indirect inguinal hernia end of each operation there is a short account of the anatomy—which the author calls anatomechanics part of the body in question, but it is not clear differs from ordinary surgical anatomy, or indeed technigrams differ from diagrams of operations cedures recommended and illustrated are all standard and acceptable

The book should be useful to house surgeons, and those practitioners who do not operate

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**British Surgical Practice Surgical Progress** (London Butterworth 1954 Pp 348 42s)—Surgical Practice keeps itself up to date by the yearly tion of a progress volume The 1954 volume is in —original articles, critical surveys, abstracts, and "n The first section is intended to remedy omissions in the work, and the ten chapters include articles on injur bile ducts by Mr Rodney Maingot on injuries of the and bladder by Mr D S Poole Wilson, and on p cerectomy by Sir Stanford Cade An excellent ch the applications of electronics to clinical practice G A Hay, shows the range of knowledge which is n needed by the surgeon The critical surveys co subjects—antibiotics, blood transfusion, carcinoma œsophagus, carcinoma of the stomach, and surgery The abstracts are of a hundred surgical papers, selected as the most important of the year's contrib surgical knowledge The noter up (a functional rath a euphonious term) shows at a glance what additi have been to chapters in the original work, and the present and previous progress volumes the may be found The chaff has been winnowed from by the editors—Sir Ernest Rock Carling and Sir Paterson Ross—and this book continues to be the g of all surgeons striving to keep abreast of their read

**Infant Feeding and Feeding Difficulties** (London J & A Churchill 1954 Pp 277 12s 6d greeted the first appearance of this book by Dr Evans and Dr Ronald Mac Keith as a very compilation for purposes of *reference* In its second it retains this character, and is even more though the authors are careful to make it clear wheth are writing with good personal knowledge of the *described or are mainly reporting* the findings of oth order not to be dogmatic they have treated at equal several methods which are dietetically equivalent, not pronounced in favour of one of them, even grounds *other than strictly* dietetic) it would hav possible to distinguish among them This comprehe and academic impartiality will appeal to the studen junior specialist Two changes of emphasis since th edition are notable On the difficult question of breas before adoption the authors, while still sitting on the now face the other way—towards the bottle Second whole exposition of artificial feeding is now based o milk instead of on liquid milk As before, almo statement of an average is accompanied by a reminde natural variability of infants, who in this book are defended against the rule of the thumb

THE LANCET
NDON SATURDAY FEB 5 1955

# Acute Respiratory Infections

hysician who has difficulty in finding his way the maze of undifferentiated acute upper ry infections will be glad to learn that more m the laboratory is on the way First news ame from two groups of workers in the U S A r a year ago ROWE et al [1] at Bethesda l that they had isolated viruses from a large of surgically removed adenoids but the of these viruses to disease in man was then n. Shortly afterwards HILLEMAN and WERNER[2] d the isolation of similar agents from Army with acute respiratory disease or A R D [3] nown as 'febrile catarrh' [4]) In the past Bethesda workers have ploughed a large area portant new field and they have unearthed teresting findings [5]

NER et al [5] tried first to define this group of and then to discover its relation to disease in Nearly two hundred strains have now been from adenoids and tonsils removed at opera- from patients with acute respiratory infections ecause of common properties these viruses belong to a single group They are all epi opic causing very characteristic changes in owing in tissue-culture they are not patho- or ordinary laboratory animals they are nt to other and antibiotics and finally they common 'soluble' antigen which is detected plement-fixation tests Within the group six t serotypes are distinguishable by virus- isation tests in tissue culture and such dif tion has epidemiological significance Forty ains of types 1 2 5 and 6 have been recovered th two exceptions all came from cultures of ls or tonsils removed at operation. The two ons were a type 1 strain which was recovered he pharyngeal secretions of a child with ive pharyngitis and a type 5 strain which rom a laboratory technician who while work h this agent developed sore throat and ear ithout pyrexia Types 3 and 4 on the other vere recovered almost exclusively from persons pper respiratory infections Type 3 virus was in a 2-year old girl with acute febrile rhinitis, gitis and conjunctivitis who was admitted to where apparently she initiated a small ak [6] Within two weeks of her admission there ven further cases five very similar to the first two with mild rhinopharyngitis, and from all of atients evidence of infection with type-3 virus was obtained The clinical manifestations comprised fever for five or six days in six patients pharyngitis in seven with exudate in two, rhinitis in seven cervical lymphadenopathy in five, and conjunctivitis in four This seems therefore to be a distinct clinical entity HUEBNER et al [5] also mention outbreaks of acute catarrhal pharyngitis and conjunctivitis among students in a summer school and their household contacts type-3 virus was found in the throat or conjunctival secretions and oral secretions of seventy-six of these patients It seems too that an agent isolated by NEVA and ENDERS [7] from a child with an illness resembling roseola infantum was a type-3 virus

Type-4 virus was first isolated by HILLEMAN and WERNER [2] from three cases diagnosed as primary atypical pneumonia and two diagnosed as acute respiratory disease during an outbreak among recruits at Fort Lennox Wood, Missouri The association of type 4 viruses with acute respiratory disease has now been further confirmed HUEBNER et al [5] recovered type-4 virus from the nasopharyngeal secretions of six military recruits with febrile respiratory illnesses resembling acute respiratory disease, and DINGLE et al [8] have studied the relation of type-4 virus to certain types of acute respiratory infections by retrospective serological methods using sera collected by the U S Army Commission on Acute Respiratory Diseases during experiments on volunteers and sera from patients clinically diagnosed as having various infections of the upper respiratory tract They found a distinct rise in antibody to type-4 virus during convalescence from acute respiratory disease and from bronchitis resembling atypical pneumonia but not from mild or severe common cold or definite syndromes of primary atypical pneumonia. Of eighteen volunteers who some years ago were inoculated [illegible] is experimentally with acute respiratory disease [illegible] lor have now been shown in retrospect to have [illegible] tive detectable antibody to type-4 virus in their pre[illegible] rva- tion sera, but antibody developed in [illegible] and contrast, of the six volunteers who [illegible] rest symptoms after inoculation five ha[illegible] Only of antibody in their pre-inoculation [illegible] on the the agent used in these stud[illegible] physical as a type-4 virus Studies [illegible] shown respiratory disease [illegible] in three [illegible] disease that in two but not in th[illegible] been an agent similar [illegible]

Outbreaks of in[illegible] physique provide the most f[illegible] work of the causal organ[illegible] on the such outbreaks [illegible] r It is logical importance [illegible] lated to communit[illegible] omorphy simple ass[illegible] Channel does not [illegible] owment In or[illegible] at the ultra[illegible] bo publish[illegible] vision of Hum[illegible] serological survey [illegible] in volunteers with [illegible] sera from a group [illegible] in three hospital [illegible] serotypes by a virus [illegible] tissue-culture Antibodies [illegible]

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W P, Huebner, R. J, Gilmore, L. K, Parrott, R. H, [illegible] T [illegible] Proc. Soc. exp. Biol., N.Y. 1953, 84, 5[illegible]
[illegible] man, M. R, Werner, J. H. Ibid 1954, 85, 1[illegible]
[illegible] ing article Lancet 1954, i, 867
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[illegible] R. H, Rowe, W. P, Huebner, R. J, [illegible] Ibid p 1057
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were quite prevalent in the young age-groups, over 30% of infants aged 6–11 months already had antibodies to these two types The findings in older children accorded with the observation that most of the viruses recovered from surgically removed tonsils and adenoids of children attending the same clinics were of types 1 or 2 Antibodies to the other four types were not so common, but there was a sharp rise in the frequency of antibodies to type 4 from 25% in those aged 6–15 to 71% in those aged 16–34 This suggests that type-4 virus may have been more prevalent in that area fifteen years ago, but perhaps such a conclusion is best deferred The volunteer studies have not yielded much further information Infected nasopharyngeal secretions and tissue culture fluids containing active virus were administered intranasally to adult volunteers Few objective signs of illness resulted, although most of the volunteers showed serological evidence of active infection No differences were noted between volunteers who had pre existing serum antibodies and those who had not

The discoveries of the past year add greatly to our knowledge of this difficult subject, but they also leave many questions unanswered In particular, there is great need for more facts about the rôle of these viruses in the host of minor respiratory illnesses encountered in general medical practice The laboratory will soon be able to help physicians by adding the complement-fixation test with these agents to the techniques for investigating respiratory virus infections If the suggestion of HUEBNER et al is accepted, this group of viruses will henceforth be known by the name "adenoidal-pharyngeal-conjunctival" agents Perhaps the best justification of this title is that it will soon be mercifully abbreviated to A P C—initials which hint at a suitable treatment

## Indices of Heat Stress

IT is not easy to assess the physiological effects of work in hot conditions The main environmental factors are the temperature, humidity, and rate of movement of the air, the amount of radiant heat, and the clothing, but equally important are the physiological factors—metabolic rate, acclimatisation, and availability of water and salt to replace losses in the sweat Of the various methods of measuring heat stress, the only one that was at all widely used until the 1939–45 war was the two effective temperature (E T) scales These scales, evolved by YAGLOGLOU et al[1–3] in 1923, have proved of considerable value, although designed as an index of comfort, they were found also to predict the physiological state They take into account the dry and wet bulb temperatures and the rate of air movement, but they made no allowance for radiant heat until BEDFORD[4] suggested that the globe-thermometer temperature should be used where this differed from the dry-bulb temperature

In the late war the E T scales were used at first for defining tolerable conditions in ships operating "closed down" in the tropics But the validity of the scales in severe conditions had not been fully tested, and the effects of clothing and acclimati imperfectly understood Research on th was therefore undertaken in speciall climatic chambers at the National Hosp Square, where it was found that, although the E T scales measured the stress accurat certain circumstances they could be mis for instance, by underestimating the d effects of still air on men working in h environments[5,6] Since it did not seem p modify the E T scale to correct these errors, and his colleagues[7] at Queen Square constructed an alternative nomogram, based o obtained on acclimatised volunteer naval This nomogram was designed to predict th logical state at the end of four hours in t conditions, the unit of measurement being hour sweat loss The predicted four hour s (P$_4$SR) derived from the nomogram was f correlate very well not only with the observ for sweat loss but also with the final rectal tures Since the pulse rate varies in parallel rectal temperature the P$_4$SR does in fact giv estimate of the physiological state as well a probable salt and water requirements

Mr F E SMITH[8] has now compared the of the P$_4$SR scale with that of the E T scale, to detailed statistical analysis some of th of the Queen Square workers He divided into four main groups according to the work clothing, and compared the two indices ability to predict the sweat losses and the temperatures On all counts the P$_4$SR scale superior or equal to the E T scale The P$_4$S more practical since it allows for the amount and the character of the clothing and guide to the amount of unevaporated sw is important in determining the degree of The E T scales measure the predicted phy effect in terms of that temperature of still air, s with moisture, which would have the sa as that of the environment under considerat relate an effective temperature to phy response it is necessary to consult graphs particular combination of work and clothi curves bear a logarithmic relation to the and rectal temperature and are very di remember This is one of the major defects E T scales On the other hand these scales to understand than the P$_4$SR scale, and th tion is quicker Moreover the E T scales wide range of environments from very cold hot, whereas the P$_4$SR scale is concerned only regions in which sweating may occur The tages of the E T scales seem to have SMITH considerably, and he has devised simple and ingenious additions to the E T no by which the amount of work is taken dir

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1 Houghten F C Yaglogiou C P *J Amer Soc Heat Vent Engrs* 1923 31 89
2 Houghten F C Yaglogiou C P *Ibid* 1924 30 193
3 Yaglogiou C P *J industr Hyg* 1927 9 297
4 Bedford T *M.R C (War) Memor* no 17 H.M Stationery Off 1946
5 Benson R S, Colver T, Ladell, W S S, McArdl J W Royal Naval Personnel Research Committ Research Council, report no 45/205 1945
6 Dunham W Holling, H E Ladell W S S Scott J W Royal Naval Personnel Research Medical Research Council report no 46/316, 1946
7 McArdle B Dunham W, Holling H E Ladell W J W Thompson M. L Weiner J S Royal Nav Research Committee Medical Research Council, r 47/391, 1947
8 Indices of Heat Stress By F E SMITH Medical Council, memorandum no 29 H M Stationery O Pp 51 2s

though again the result is given in terms of ure These additions are founded on the f the Queen Square workers, but only at of metabolism, and thus the new nomogram l largely from intrapolated and extrapolated In doing this SMITH has made the question mption that in all environments increase ears a linear relation to the resultant increase logical effect Until an accurate and fully nsive scale can be constructed embracing nments and including extremes of heat and ould perhaps be wiser to use the P4SR scale if conditions are not severe the E.T. scales ove reasonably satisfactory

## Body-build and Temperament

ea that a man's body build is related both mperament and to his proneness to disease om now The difficulty in testing this idea to devise good objective methods of recording The Hippocratic division into *Homo* s and *Homo apoplecticus* was a useful first ation. Others since then have been content ognising continuous variation, to make the vision between those who are relatively their height (leptosomes, asthenics) and those heavy (pachysomes, pyknics) REES and ,[1] for example following BURT in the use analysis, found in a sample of soldiers one actor for general body size and another ype factor contrasting length with width umferential measurements But as is well o boxers and wrestlers the same height atio, even in well trained men with little include physiques which differ widely in strength and skeletal form and a satis classification must include some estimate variation HAMMOND[2] has applied factor to measurements of British and American . He too found a general size factor and a tor distinguishing those excelling in length se excelling in circumferential measurements ddition in boys he found a second type factor istinguished those who were rotund and not y broad (excelling in circumferential measure fleshy parts, but with relatively small bones) ose who had a broad trunk and big bones. more intuitive approach SHELDON[3 4] dis- es between three components of physique have much in common with HAMMOND's , except that SHELDON is not concerned with size His components are (1) endomorphy rised by ready accumulation of fat deep ound skull and thick upper arm and thigh atively thin wrists and ankles (2) meso- characterised by big muscles and bones ut not thick chest cubical skull, and large s and calves in relation to upper arms and and (3) ectomorphy characterised by linear arrow chest narrow face long thin limbs, t bones SHELDON types a person by giving core for each of the three components. This is objective in that independent observers will arrive on about the same grading from measurements on a correctly taken photograph The somatotype has been shown to remain more or less constant in adult life, though it is not yet certain whether it can be estimated accurately in childhood

Full understanding of the constant elements in body build will come only when the genetic factors have been determined but this is no reason for not trying to associate temperament and disease-proneness with linearity of build or with SHELDON's somatotypes The first more or less scientific attempts were those of KRETSCHMER who distinguished between pyknic athletic, asthenic, and dysplastic types He found that the pyknic were especially liable to have a cyclothymic personality and to develop manic depressive psychosis, whereas asthenics were especially prone to schizophrenia While some psychiatrists have confirmed his findings others have not—partly, no doubt, because his assessment of physique was too subjective REES[5] related the score in his second factor—that of linear or stocky build—to neuroticism in soldiers and found that hysterics tended to be stocky, and obsessionals and those with anxiety states to be linear SHELDON[6] has related his three components of physique to three components of temperament—viscerotonia somatotonia cerebrotonia—which are associated with endomorphy, mesomorphy, and ectomorphy respectively Viscerotonia is characterised by qualities which include complacency, love of comfort enjoyment of food, need of affection, and sociability somatotonia is characterised by assertiveness pleasure in bodily action and insensitivity to pain cerebrotonia is characterised by restraint self consciousness sensitivity and love of solitude Gradings for these qualities of temperament are not as objective as the gradings for physique but common observation suggests that the associations are real ones, and as objective tests become available it will be interesting to see how they correlate with physique Only preliminary reports have so far appeared on the association of somatotype with mental and physical disease For example GERTLER et al.[7] have shown that those who develop early coronary artery disease are usually endomorphic mesomorphs

An interesting sidelight on associations of physique with temperament has come from the work of TANNER[8] and PARNELL[9] in this country on the relation of somatotype to choice of career It is natural that choice of sport should be related to physique no one who is not high in mesomorphy could hope to excel at rugby football while Channel swimmers usually have a considerable endowment in endomorphy as well as in mesomorphy But the association of somatotype with occupation is presumably mostly through temperament In the U.S.A. GARN and GERTLER[10] showed that workers on the floor of the factory tended to be lower in ectomorphy and higher in the other two gradings than those in the research departments This was not a social class or educational difference since the men on the managerial side of the factory differed even more

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[5] Rees, W. L. *Eugen. Rev.* 1947, 39, 31
[6] Sheldon, W. H., Stevens, S. S. The Varieties of Temperament. New York, 1942
[7] Gertler, M., Garn, S., White, P. *J. Amer. med. Ass.* 1951, 147, 621
[8] Tanner, J. M. *Eugen. Rev.* 1954, 46, 149
[9] Parnell, R. W. *Brit. med. J.* 1953, ii, 472
[10] Garn, S. M., Gertler, M. M. *Amer. J. phys. Anthrop.* 1950, 8, 38

from the research group in their relative lack of ectomorphy In this country TANNER[8] has shown that officer-cadets at Sandhurst are on the average more mesomorphic and endomorphic than undergraduates at Oxford, while preclinical students at a London hospital were intermediate between the Sandhurst and Oxford groups PARNELL[9] has found that at Oxford medical students are more mesomorphic than the remainder, and that at Birmingham dental and engineering students are more mesomorphic than students of physics and chemistry Moreover, the whole distribution of somatotypes at Oxford is more central than at American universities studied by SHELDON The extreme mesomorphs and the extreme ectomorphic endomorphs were absent from the Oxford group, and there is a relative shortage among them of extreme ectomorphs These studies relate somatotypes to choice of, and selection for, career, but association with success in career is of greater practical importance As a first step PARNELL[11] has attempted to relate the somatotypes of Oxford students to the type of degree they achieve in the final honours examinations His numbers are small but suggest real differences Notably there is a tendency for those predominating in mesomorphy

to get their fair share of first-class
relatively few thirds, the great majorit
seconds Understandably this group were
to have made the biggest contribution to
sport The highest proportion of firsts
near-central endomorphic ectomorphs The
ing findings need confirmation and further
one possible source of confusion is that fir
awarded more generously in some subj
others There is no reason to suggest th
is in any way related to intelligence, and
type is related to academic success
through temperament Perhaps the highly
among extreme ectomorphic
insufficient energy to get to the university
intelligent extreme mesomorphs may pref
their powerful grip on adult life early witho
time on non-vocational education.
moderately high mesomorphs, if they g
university, have sufficient drive at least to
a second, but may be too restless to get a fir

The basis of these probable, though
proven, relationships between physique,
ment, and proneness to disease is uncertain
of the association may be basically genetic
to the multiple effects of single genes

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[11] Parnell, R W *Brit med J* 1954 ii, 491

# Annotations

## MALARIA IN THE AMERICAS

THE inception of a five year campaign to eradicate malaria from the entire American continent has been announced by the Pan American Sanitary Bureau, a subsidiary of the World Health Organisation The extent of the undertaking can be judged from the fact that 135 million people in the Americas live in potentially malarious areas—60 million in regions where the disease has been suppressed, 45 million in "protected" zones, and 30 million in unprotected areas The aim is to extend control to all the malarious regions, and to intensify it to the point where transmission ceases If transmission can be prevented for a few years gametocytes of *Plasmodium falciparum* or *P vivax* will not recur and the disease will disappear

Twenty years ago such a scheme would have been fantastic But the residual insecticides have made possible very large and successful antimalarial campaigns—for example, in the Mediterranean, in the U S.A , and in Ceylon The highest levels of control have been achieved in the more temperate climates, where both the plasmodium and the anopheles are seasonally checked by cold Much of the American territory already conquered falls into this category, whereas it is not unlikely that the areas at present "unprotected" from malaria are tropical, undeveloped, and largely inaccessible Furthermore, recent events in Central American States suggest that political unrest may hamper international operations

In most previous campaigns there has been only one main vector to attack But in the vast American territory many different anophelines predominate in different regions (e g , *A freeborni*, *A quadrimaculatus*, *A albimanus*, *A darlingi*, *A* (*K*) *bellator*, and *A pseudopunctipennis*) The problem of suppressing transmission is different with each of these mosquitoes Their very diverse breeding habits are probably unimportant, for it is almost certain that they will be attacked in the adult stage by residual insecticides The most important characters of the insects are (*a*) their "domesticity" (i e , whether they bite man in or near houses and will
rest on treated walls), (*b*) their sensitivity
insecticide, and (*c*) the possibility of their d
insecticide-resistant strains Resistance to
is a serious hazard for which we must remain
Greece, insecticides gave perfectly satisfacto
for several years, but last year malaria was
in 144 villages owing to resistant strains of A

Malaria eradication, though not so difficult
eradication, demands much more effort th
control An attempt at complete suppression
such a vast area as North and South America
for all the optimism and drive traditionally
with the New World

## INTESTINAL OBSTRUCTION IN THE

AIR is the most useful contrast-medium for the
of intestinal obstruction in the newborn infa
ingested with the first breath and passes
the stomach into the small and large bowel
and Jester[1] have reinvestigated the rate of
air in a series of normal and premature babi
might be expected, they found considerable
Within the first two hours all the babies had
small bowel, and in 50% it had already passed
cæcum or ascending colons By six hours the
and descending colon were filled, but the fil
sigmoid and rectum was inconstant, air show
sigmoid in 82% at six hours but in only 25%
hours Podolsky and Jester concluded,
enough, that flatus must have been passed p
for air reaccumulated over the next few h
premature babies the air tended to progress mor
one infant weighing 4 lb 8 oz had air in the
hours and thirty five minutes after birth

The value of a plain radiograph of the ab
localising intestinal obstruction will therefor
largely on the time at which it is taken Du
high intestinal obstruction may be recognis
a few hours after birth, whereas obstruction lo
the alimentary tract may not be apparent un
five or six hours after birth Podolsky and Jes
on the importance of lateral films, particularly
nising the rectum and sigmoid, since loops of

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[1] Podolsky M. L , Jester A. W *J Pediat.* 1954,

the pelvic brim and on an anteroposterior film mistaken for the lower bowel The distribution the intestine is not the only diagnostic feature resence of an obstruction will lead not only to passage of air but also to gaseous distension of l, and this gives rise to characteristic appear h as the gross distension of the stomach and of the duodenum in duodenal atresia Radio ust always be taken with the infant upright rectal atresia when the patient must be inverted tallic object placed in the perineum so that the een the gas filled lower bowel and the skin may ated Barium by mouth has no place in the tion of the newborn infant and it may be s if there is vomiting But a barium enema is for the diagnosis of low intestinal obstruction Hirschsprung's disease for there is no other of recognising the typical narrow segment [1]

y of the newborn infant has advanced strikingly ast decade, and more accurate diagnosis of l obstruction by radiography has played no t in this progress

## DIETARY SODIUM RESTRICTION

U.S.A the value and dangers of dietary sodium n have been concisely and authoritatively sed in excerpts from a report prepared by a small e for the Food and Nutrition Board of the Research Council and the Council on Foods and n. The first excerpt [2] deals with the physiology n, and the *normal response to sodium restriction* ond [3] shows how the indications for sodium m have been extended since in 1901 Achard and first appreciated the connection between salt d the formation of œdema in cardiac failure In to cardiac failure, the conditions in which sodium n may be of value are now held to include sion renal disease, cirrhosis of the liver toxæmia nancy and Ménière s disease The report is ely enthusiastic about restriction of sodium in edema œdema relating to cirrhosis and toxæmia nancy The verdict on the value of restriction in sion and Ménière s disease is hot proven — carries the stigma which in fact if not in theory h such a verdict The dangers of sodium restric n general treatment for renal disease are empha n relation to the possibility of 'salt losing s," and the appearance of a low salt syndrome, ydration and a precocious increase in the blood el. The report points out once again that in the at of œdema the *restriction of sodium must be* , with a daily intake not exceeding 500 mg quires a considerable effort by the doctor or n in planning the diet and a greater effort by the in consuming it ; *the labours of both (in America)* e lightened by the requirement of the Food and dministration that foods in such a diet shall be with their sodium content per 100 g and per ; and apparently *such foods* may be had in

tunately painstaking adherence to such a diet l to achieve its objective and may even lay the open to hazards [5] including inadequate general n and vitamin deficiencies ; and a greater range sodium foods and the administration of vitamin ents are recommended The sodium depletion ne' may appear especially when a low sodium conjoined with *mercurial diuretics or when* or central heating provoke significant sodium loss in the sweat and the report recommends that the serum sodium level should be checked weekly or even more often Loss of responsiveness to mercurials and dehydration *with a rising blood urea level* may also be due to excessive sodium restriction

On this side of the Atlantic we are generally less rigorous in demanding sodium restriction We try to atone for our shortcomings with mercurial diuretics, or with cation exchange resins to bind *some of the dietary* sodium after it has fulfilled its office of seasoning our food But occasional patients derive psychological strength from a strict regimen and it is perhaps in them that we should look more closely for the harmful side-effects less latent in a low sodium diet.

## ANAEROBIC COCCI

ANAEROBIC cocci are common commensals of man but they are all sensitive to penicillin and *so are not of great* pathological significance today Formerly *the anaerobe Streptococcus putridus* was recognised as an *important* cause of a dangerous kind of puerperal infection This organism and closely related strains still comprise the commonest group found in puerperal pyrexia and they are probably the cause of other forms of suppuration—for example anaerobic streptococcal myositis In the days before penicillin reduced the pathological significance of the anaerobic cocci these organisms were in a sense 'unpopular' with bacteriologists. Partly this was because in many laboratories methods for isolating anaerobes in pure culture were not part of the routine and partly because critical study often disclosed that cultures of cocci thought to be obligate anaerobes were only facultative anaerobes But perhaps the chief reason why the anaerobic cocci were not welcomed as objects for study and identification was that their taxonomy was chaotic : the most widely accepted scheme of classification comprised eight genera with thirty two species and several subspecies Many of the species were so poorly described that their names could not be justified and some of the criteria for differentiation of species were so questionable that the whole picture appeared confused in any light Still worse the biological characters of a single strain were liable to change unpredictably between one laboratory and another and even within a single laboratory between one batch of medium and another

Bacteriologists owe a debt of gratitude to Prof Ronald Hare and his colleagues [1-3] who have done much not only to bring order into the taxonomy of the anaerobic cocci both gram positive and gram negative but also to explain the reasons for some of the variability in the fermentation and other reactions of these organisms It now appears that the exact composition of the medium and choice of test substrate is very important : sulphur compounds are required for gas formation by some strains fatty acids must be present in the medium to allow other strains to show fermentative activity and still other strains can attack organic acids but not carbohydrates With media containing peptone agar or digest broth, enough of some of these substances may be present as impurities in some batches and absent from other batches to account for the hitherto mysterious variability in the reactions of the anaerobic cocci

By methods and in media which they fully describe Hare et al have examined 233 strains of anaerobic cocci Of these 141 were commensals isolated from healthy people—from such situations as the nasopharynx mouth skin intestine, and vagina The remaining 92 strains came from material aspirated at bronchoscopy (10 strains) abscesses in lungs removed at operation (3 strains) sputum from cases of chronic lung infection (10 strains) the genital tract of cases of puerperal pyrexia (60 strains)

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L. M. Stephens F D Ward B C. H Lancet 1949 i 6.
er med. Ass 1954 156, 1081
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d C. Loeper M C R Soc Biol, Paris 1901 53 346
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1 Hare R., Wildy P., Billett F S., Twort D N J Hyg Camb 1952, 50 295
2 Wildy P., Hare R. J gen Microbiol 1953 9 216.
3 Thomas C. G A. Hare R. J clin Path. 1954 7 300

and other forms of infection (9 strains) Of the 233 strains all but 27 were classified in one of nine groups based on the fermentation of five carbohydrates and five organic acids From the results of this work it is now evident that each area of the human body tends to possess a rather restricted number of groups of anaerobic cocci The strains of group 1, which correspond to the species named *Streptococcus putridus* (Schottmüller), seem to have more certain claims to pathogenicity than those of groups 2–9 But most of these strains will ferment carbohydrates or organic acids such as pyruvate, as a result they may so increase acidity as to impair the antibacterial efficiency of local defensive mechanisms In this way the anaerobic cocci might promote infection with other organisms present in the same situation, and so might be more important than is generally supposed

## PROTECTION AGAINST IONISING RADIATION

THE injuries from ionising radiation can be classified into two groups—deep and superficial Of the deep injuries damage to reproductive organs and blood-forming tissues are particularly important Experimentally malignant tumours have been produced, and in radium and X-ray workers the incidence of leukæmia is significantly higher than in other medical workers and the general population Superficial injury most commonly involves the hands, and the lesions have included epilation, telangiectasis, necrosis, and carcinoma

In his presidential address to the section of radiology of the Royal Society of Medicine, Dr J F Bromley[1] described some of the ways by which, in the absence of simple precautions, a considerable radiation risk can arise in routine hospital practice He recalled an investigation some years ago in a gynæcological ward, in one corner of which were grouped "for convenience of nursing" seven patients undergoing radium treatment Films hung at intervals along the walls of this ward recorded, over five days, dosages ranging from 0 1 to 3 0 rœntgen units, the total radiation to which the nurses were exposed must therefore have been dangerously high He pointed out that unnecessary exposure of nurses to high doses may take place during "back rounds," or as a result of over-solicitous attention to patients with implanted radium during recovery from an anæsthetic To obviate these and similar risks, he said, all procedures that had to be carried out near these patients should be executed as speedily as possible, and hospital matrons must be fully aware of the importance of keeping the numbers of nurses engaged on "radium duties" up to establishment

Effective screening of those at risk is seldom possible Formerly it was accepted that a worker could safely receive up to 1r per week, but in 1950 the International Commission of Radiological Protection put the "tolerance" dose at 0 3r per week, measured in air, for whole body radiation, and at 1 5r per week for the hands and forearms

To check that the tolerance dose is not being exceeded specially prepared films or small pocket ionisation chambers, measuring dosages as small as 5–10 milliroentgens, can be carried, and it has been usual to do routine three monthly blood-counts Various workers have shown gross correlation between blood changes and definite over exposure[2–5] Mole[6] has now made a critical survey, in an effort to determine the value of blood-counts in defining damage to the blood forming organs before irreparable harm has been done The possible changes in the blood count might fall into three groups

(1) A decrease in the count without contin
where the blood forming tissues are not irrepara

(2) A sudden terminal fall, where repair has k
destruction until the ability to repair is exhausted

(3) A gradual fall, assuming that the abili
diminishes with extension of marrow damage

In practice it appears that the changes o
of one of the first two types, which suggests
blood counts can be of only limited value L
irradiated some guineapigs at eighty times an
twenty times the normal tolerance dose In
group the white blood cell count fell by 50%
latter by only 20%, and in neither group was th
sive decrease in cell counts to indicate irre
damage Yet at the end of two years the
among the guineapigs which had received the
was twice that of controls Apparently ly
at least as common a sign of damage as n
but even with gross damage neither may be
in one case of aplastic anæmia due to radiatio
blood cell count was 4700 per c mm on the d
In any one person the white blood-cell coun
considerably, and it takes time to establish
base line Furthermore Mole questions wheth
in the number of white cells in the periphe
related to the extent of the underlying marro
and he suggests that any changes in the whit
counts of radium and X ray workers are m
be due to factors other than radiation The
cell count, he concludes, cannot be relied on t
warning of serious damage

## SKIN TESTS IN ASTHMA

ASTHMA is notoriously difficult to treat, and
of treatment are hard to assess hence the
of remedies, and of opinions on their val
testing followed by desensitisation may seem
well as simple, but this method rests on two
assumptions (1) that attacks are caused
with allergens, and (2) that skin tests can ind
allergen is responsible While the former
may be correct in certain patients, the lat
unproved

Herxheimer et al[8] have investigated the sk
in 300 patients with allergy affecting the
system, and 100 normal people More tha
patients had asthma, and the remainder
rhinitis or hay fever The "prick" test was
twelve extracts of allergens One or more of th
gave a positive reaction in 95% of the patient
in 50% of the controls In 21 patients the
repeated on different days, and the results were
in only 3, in the rest variations were consid
patients were judged to be definitely sensit
or more specific allergens, but in 6 the sk
react to the incriminated allergen, and in t
remaining 45 at least one skin reaction did
spond with the clinical evidence Herx
conclude that skin-testing cannot be relied o
a causal allergen They suggest that it shoul
in only two circumstances (1) where sym
thought to be due to non allergic causes and a
negative result would give helpful confirmat
(2) where in a suspected allergic disorder th
other evidence of specific allergy In this s
of case positive results may help in selecting
for direct testing of the bronchial or nasal
though, as Herxheimer et al point out, the
mucosa and the skin do not always react to
allergen This work suggests that skin te
scarcely any value in these common respirator

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2 Goodfellow, D *Brit J Radiol* 1935 8 669 752
3 Helde M *Acta Radiol Stockh* 1946, 27 308
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Utidjian H M D *Acta allerg Kbh* 1954 7,

# Special Articles

## REDICAMENT OF THE FAMILY IN THE MODERN WORLD *

HENRY V DICKS
M.A M.D Camb F.R.C.P
TO PSYCHIATRIST THE TAVISTOCK CLINIC LONDON

than twenty years ago Ogburn [1] in the U.S.A hat the rapid alteration in social and techno nditions had profoundly affected the economic ad even the personal aspects of family life But he *family is everywhere exposed to change and* chment by other institutions (e g the State) mains the social atom—the irreducible unit of ganisation Why? Because the human infant re than any other living creature is endowed biological need for the intimate experience of rotective mothering Hence the human mother l many animal mothers requires the security of tself satisfied and cared for in order to answer l in the infant For this bio psychological func e conjugal family there is no adequate substitute ties safeguard it by marriage customs The tion and adaptation to changing conditions of this l institution is the prime consideration of all of rned with mental and communal health

### FAMILY TENSIONS AND MENTAL HEALTH

n psychological discovery has demonstrated in ting fashion that for the human child other beings especially the mother, are the most nt factor in the environment and there can no e much doubt that broadly speaking healthy levelopment is founded on an infancy spent in a e, stable, loving family The reverse side of the —psychopathy and neurosis in deprived children— more fully documented, and we are all becoming f the links between unhealthy emotional con n people's childhood and their later psychological onomic nervous disturbances Psychopathology happy parent-child relations are, in a sense ble

intensive personal studies of a large number of marriage failure I can confirm that there is a nt relation between an unhappy family back of the spouses and their incapacity for a good e relationship [2] This is also found in Slater and nd's study of London working class marriages in and *non neurotic samples* [3] The crucial factor o be not a physical break by death &c in their d home but rather the images and memories of *unhappiness* These images and memories may ension in the minds even of people who show te adaptation in all other spheres of life Marriage most special and intimate human *relationship* to light neurotic faults and distortions of per which can remain undiscovered in other less g situations—even in war experience

Psychic processes which interfere with good marital *s appear to me to stem from disappointment in* tion of how the marriage partner should play his exual marital role I find that people who are d to fail in marriage love and marry not a real person but a more or less distorted image of inner fantasies projected into the partner The projected image may represent repressed aspects of the subject's own personality or more frequently the residues of still potent internalised parent figures Unhappiness and recriminative behaviour in open or concealed form break surface because the partner does not answer the secret wish for a parent surrogate Intimate contact reveals the lack of capacity for dealing with the real partner in a mature and tolerantly loving way and demonstrates the immaturity or crippling of the emotions which have developed only to the level of the ambivalent demanding (because deprived) child Once there develops this neurotic attitude towards the marriage tie it tends *to invade other spheres of life of the individual : parenthood* work and capacity for enjoyment Escape patterns and neurotic defences are mobilised in all the familiar forms

Even if they attempt it the disturbed couple can rarely conceal their tension and hostility from each other or from their children Children internalise in love or in fear and anger what they see and feel about their parents just as the parents had internalised the unhappy angry forbidding images of *their* parents In this way the deprived child is likely to become an unsuccessful marriage partner in his turn Thus an increase in the incidence of marital breakdown in a community will directly swell the numbers of conflict torn insecure children who have not learnt to identify with good parents Because they have not done so they will be unable *to give out secure affection in adult life as fully* as they should in their marriages or in the wider sphere of social obligations. I need not labour the danger to society if this were allowed to go on unchecked It would be ironical if we were to see an advance in physical well being (due to our efforts at public education and hygiene) go hand in hand with a disintegration of social and personal relationships—i e, of mental health

My experience based on the observation of guilt feelings in unhappy marriage partners and of their attempts to improve their relationships and to protect their children from the effects of their conflicts leads me to think that deep down most of mankind cherishes the values of marriage and of the happy secure family as perhaps the greatest and most natural source of a sense of satisfaction and personal worth We have to seek the causes of the disturbed or broken marriage in the development of their personalities *under given social* conditions

### THE MODERN FAMILY

A generation ago we might have been moved to say that we needed an army of psycho analysts to help these unhappy people by individual therapy—both of parents and children That they need help and treatment remains just as true today but we have now begun to broaden *our concepts of mental ill health to include not only* personal but also social aetiology I propose to offer some ideas on the possible connection of the disquieting phenomena of increasing marital instability and divorce in Western societies with the rapid changes in our communities We know that there were marital unhappiness parental neglect crime mental disease and brutality in every epoch of history Our concern and our awareness of it in our era are due to the development of the psychological and social sciences which have made us think of these matters as coming within the realm of research treatment and prevention—just as the development of general medicine and hygiene have made us think of epidemics and of surgical catastrophes no longer in terms of inevitable calamities but of controllable events Our thinking may be still tentative because our knowledge is limited It is important that we here affirm

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ubstance of a paper given in the technical section for mmunity Organisation for Mental Health at the Fifth ernational Congress for Mental Health, August 1954 Toronto Canada.

rn, W F In vol II of Recent Social Trends in U.S.A York, 1931

h, H V Experiences with Marital Tensions in the Psychoal Clinic *Brit J med Psychol* 1953 26 181

r E, Woodhead M Patterns of Marriage London 1951 the similarity in principle with general hygiene And we know enough to propose action with modest confidence in some areas

In traditional societies such as are still the rule in many parts of the world, as they once were in Western Europe, the family or kinship group conferred economic autonomy, division of labour, and human security and companionship Its functions were an integrate of economic, cultural, and personal cooperation as an aid to survival This large primary group shared values, and religious and leisure life The rôles, duties, and obligations of each kind of member were clearly defined by custom and taboo Thus such a family was not only a rich and meaningful milieu it was also often the *only* milieu—school, workplace, and transmitter of the cultural heritage from generation to generation Because of the variety of figures who composed the group, it was possible for each member to spread his loves, hates, and many other emotions between parents, grandparents, uncles, aunts, cousins, and siblings, yet within prescribed limits It was a narrow but a safe world—each knew his place and status

The modern urban family with few children, which social mobility has now made typical of our Western society, is a much shrunken successor to this traditional kinship group It has developed rather quickly—over only a hundred years or so—and thus it shows many contradictory or conflicting stresses within it Technology with its demands and opportunities has imposed its values on such a family The children are expected to surpass the parents in education and skills, and often to found their own families far removed in physical and in social space from the parent generation The development of dormitory suburbs around the new industries, &c, into which newcomers settle, or into which families move as part of "slum clearance" schemes, has produced a degree of social isolation or atomisation, where each little family may remain, and often feels like, an island amid a "sea of strangers" Social mobility and rootlessness may drive many young men and women who have grown up in such a milieu to marry each other from no deeper motive than loneliness This is the social aspect of the marriage in search of parent substitutes The monotony of industrial working life and the lack of wider social relations now drive the couple and their too few children to expect most emotional satisfactions from each other—with the consequent exaggeration of emotional demands The marriage is expected by the partners to supply them with all the relational security previously spread over a wider and varied kinship group several generations deep The intensity of feeling is passed on to the over valued children who are having to work out their developmental emotional conflicts within this limited "psychological space" Moreover, urban life, with its real dangers, and its cramped living conditions for the majority, makes a small child's adventures into independence a matter of anxiety, and often a cause both for over-protection[4] and for resentment by the parents, who would like to feel free to indulge their unsatisfied cravings for the "good life" among the attractions of the city

For the fortunate minority, life in big cities does indeed offer opportunities for wide and varied experience and social relations This minority perhaps attains in our civilisation a breadth and a universalism undreamt of in former days This limitlessness of development is in theory open to all, and justifies the loss of the old securities But it can be achieved only if emotional background at family level, coupled with good abilities, has adequately equipped the personality for metropolitan life As yet there is fear of freedom, and
even escape from freedom, because in
personal responsibility Such is the contrad
the present urban family pattern Technolog
demands personnel trained to independen
reliance The family, in its isolation from
outside contacts, still asks from its children
virtues of dependence, it clings to the childr
the parents live vicariously through the ch
neither generation has other kin to fall bac
values which the parents' parents hold ar
those of the children

This process is not perhaps so clearly se
long urbanised communities who have
tions to this way of life—such as in Viennese, P
Londoners It is very marked in new com
such they can be called), where the housewife
is driven into conflict owing to loneliness, with
at the factory all day and in no mood to share
burdens when he comes home She resents
child dominated life, and is unconsciously
towards her social role The children inter
what little pleasure she and the husband may
before their arrival She may take out her
on the children and on the husband, and bot
begin to long for escape No traditional ties
but only inner loyalty and personal respons
there to help stabilise them[5] Moreover, the
has introduced a conflict of sex rôles into the
married women, because it offers equalities of
as workers and competitors with men

It is the experience of medical practitioners
that in secure, old-type rural communities
much less common than in dormitory
F A Bevan[6] has stated that in his practic
quarters rural, a quarter industrial settlement
all the problem children, the marital difficulties
neuroses come from the industrial families

Modern child psychiatry has long recogn
stress in a family cannot be compartmental
know that the whole unit is involved, even th
one member may present himself as a patient
is brought because it steals or cannot do its
this is only the symptom Behind it we ofte
mother incapable of responding to her chil
because she resents the tie of husband and chil
husband responds by unfaithfulness or alcohol
variants are infinite, and well known to phys
lawyers The weight of symptoms does not al
on the most pathological personality among th
The person who acts out his aggression does not
as the victims

Obviously, I have generalised from a conden
clinical experience There are many happy, well
urban families We have to find out what keeps
But there is also much concealed family te
suffering Only some of it bursts into the open
psychiatric form Family doctors, derm
industrial medical officers, gynæcologists, mag
divorce court judges, pharmacists, clergy, te
saloon barmen see different and earlier asp
There is no doubt in my mind that the rathe
change in kinship structure and emotional "
ness" which the Industrial Revolution and its c
social mobility and urbanisation have brough
accounts for a great deal of the malaise in fam
not to speak of the destructiveness of mod
which themselves reflected the discontents of

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[4] Overprotection on the part of ambivalently anxious parents is psychologically also a "deprivation"—of the child's normal need to assert its independence

[5] We may compare the change from traditional to moral sanctions to the biological processes of exoskeleton and developing an endoskeleton.

[6] Bevan, F A Contribution to discussion on Family and the General Practitioner British Medical annual meeting Cardiff, 1953 Unpublished

cott Parsons [7] has pointed out the nature of this kinship situation for the American nation

### THE COUNTRIES OF RAPID CHANGE

ve reflect that the stresses and strains centred mily are great and potentially destructive in societies, what can be the prognosis for those "undeveloped" communities which almost have begun to industrialise and to attract ibers away from the land from kinship systems ure patterns much more compelling and less listic? After all Western culture has developed nd—at least since the break up of the feudal has emphasised the conjugal family as the unit structure Under the authority of Christian it has been accustomed to regard the free ip of husband wife, father mother rôles as the *motional security*

will happen in the minds and feelings of scores nds in India, China or Africa now pouring out ir villages into new industrial towns? How make sudden breaks with their different culture of marriage, oriented around different values and systems?

so new centres of industrial change we shall need *plicit agencies of mental hygiene and welfare* urgently as, in the cities now rapidly enlarging e this flow of—yes—displaced persons we shall er public health installations such as drains and ters and inoculation stations

not competent to speak in detail of the effects of gical change on non European societies but ple, it would seem that wherever modern industry in settlement appear there old kinship systems p and the small conjugal family becomes the unit for the security and emotional satisfactions embers, parents and children. We know what it is subject to It therefore becomes the focus r mental hygiene We are likely to see repeated he same phenomena as have accompanied the ation of women through industrial work in and the same relative diminution in assured edominance These will be due to the intensifi f conflicts and doubts in the playing of the sex etween traditional internalised parental standards pressures of present reality The first generation be so badly off but the full impact may well fall children

social and economic policies which ignore or ene the optimal transition from the traditional *ictual kinship situation will increase this conflict* and new values and pressures and lead to wide marital catastrophes broken homes and derelict without stable values and without safe good to identify themselves with

perhaps already too late in many areas to avoid just as in the Soviet Union rapid forced indus ion with its concomitant deliberate loosening of ties led to the tragic phenomenon of the *bezpri* children in the early years of the régime com the authorities to a complete turnabout in defence old fashioned family mores

### ACTION?

e are in my opinion two levels of possible action

TM

is politico-social planning for the creation in the ban communities of effective (if at first artificial) utes for the kinship group—to make the factory o settlement round it a friendly good neighbour in which from the start the working families can feel supported and have a plot of garden to cultivate to prevent rootlessness and *Lumpenproletariat* deterioration[8] with facilities for adult education in skills in the new living including parentcraft All the social sciences—psychiatry psychology, anthropology, sociology and economics—must be brought to bear on solving the problems of each such new centre in terms consonant with the history and traditional culture pattern of the people as a whole But this is not enough The goal cannot be the creation of shepherded supervised, and welfare minded" communities. That is only for the period of acute dislocation and readaptation We surely want communities so structured as to be secure and mature enough to progress towards self management and democratic responsibility

Furthermore—and this applies to Western as well as to new communities—we need to work out a consistent policy based on mental health values, in regard to families. Our clinical insight tells us that young children must have safe and continual mothering But our fiscal and economic trends as well as the emancipatory revolt of urbanised women pull the young mother away from her maternal rôle The State tends to supplant the parents as the providers of goods and services to the children At what point and in what cases do we intend *to say that the break up of the multi generational family* makes for personality development and is good and where does this break up become malign because it prevents the assimilation of good devoted security giving parent figures by the children? Such optimal points between care and independence need to be worked out for each community

*Short term*

We shall have to act in several ways and quickly The 1948 International Congress for Mental Health adopted a statement which described three phases in the development of mental hygiene action [9]

The first consists in segregation and custody of the severest forms of lunacy and idiocy with psychiatric thought confined to the descriptive Linnæan level Many communities have a bare sufficiency of services even in this respect

The second developed after the first world war in some Western countries and concerned itself with therapy—including that of neurosis. Early treatment centres and outpatient work in a broadly psycho-analytic spirit appeared This work gave impetus to research and thought on the ætiological level, which was also fed back into improved provision of therapy and teaching in *mental hospitals Such provision for treatment must be* made—not necessarily in slavish imitation of what has been done in Western countries It will give us research and teaching centres as well as treatment facilities It will be a demonstration of what help can be given and on what theoretical concepts mental health action is based

But the focus of effort should be directed to the third phase—the sending of this trained personnel into the public health services *in the community* In family and child clinics in mothercraft training in industrial welfare and so forth When the usual and well recognised workers in community health—the family doctor the public health staffs and maternity nurses the teachers and the administrators—can adopt the view point and use the skills of the mental hygienist and can see the interaction of society and personality then we shall have begun the work of real prevention

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[7] ons, T. Essays in Sociological Theory Pure and Applied ncoe Ill., 1949; p 233

[8] The economic pull of industry will and is often—regrettably—permitted to lure young fathers away from village homes into barrack life without regard for human misery

[9] Proceedings of the International Conference on Mental Health London, 1948 Statement of International Preparatory Commission, in vol IV (p. 5) London

# THE SUTTON COLDFIELD RAILWAY DISASTER

## Evacuation of Casualties

In the derailment of the York-Bristol express at Sutton Coldfield on Jan 23, 17 people were killed and 41 were seriously injured With the considerable resources of the Birmingham area within ten miles, it was possible to treat this number of injured with no more than a spurt from the normal casualty machinery of the local hospitals The first stages of the prearranged plans for dealing with a major catastrophe in the area were in fact put into action, but it turned out that the hospitals were able to cope without taking any of the later steps that had been agreed upon

Last year [1] the Ministry of Health suggested to hospitals and local health authorities some ways in which their organisations for dealing with big accidents might be improved, and the effective handling of the casualties at Sutton Coldfield has again illustrated the importance of detailed preparedness The emergency plan which had been decided upon for the Birmingham hospitals had been drawn up in cooperation with the police, the ambulance authorities, the general practitioners, the industrial medical officers, and the voluntary organisations This was, of course, only a part of the response evoked by this particular accident, the greater share being contributed by the organisation for Sutton Coldfield itself, and particularly by the local general practitioners, but it may be useful to summarise some of its provisions, which no doubt are much the same as those that have been agreed to in other parts of the country

### *The Birmingham Plan*

A major catastrophe is defined as one involving 50 or more seriously injured casualties, *or* one that is determined as such by the duty officer at the fire and ambulance control centre in the light of the circumstances The decision as to whether the plan should come into operation is thus the responsibility of the duty officer at the control centre, though he will consult if necessary with the medical officer in charge of casualty services (who will go to the spot) and the medical coördinating officer (who will go to the control centre)

When a catastrophe is declared, it is the task of the hospital services to provide (*a*) a team or teams of doctors and nurses, with equipment drawn from hospitals, to join in setting up first aid posts at the scene of the accident, and (*b*) a medical officer in charge of the casualty services, who will organise and direct first aid on the spot, and pass back information about the nature and number of the casualties to the medical coördinating officer, who will ensure that the first-aid teams get what they want and that the casualties are taken to the hospitals best prepared to receive them

At the same time the police will send two wireless cars to the scene and establish an "incident post" which will be in touch by telephone or wireless with the control centre and the central police information room The police will also provide a limited quantity of first aid equipment It will be their responsibility to record the names and addresses of those involved, and to give information to inquirers at the scene or via the police information room ("The importance of the police obtaining such information cannot be minimised, but on no account will ambulances be delayed for this purpose") If necessary the police will arrange special mortuary accommodation near the scene

At the outset the duty officer at the control centre will tell the doctors and administrators chiefly concerned what has happened, and he will direct to the scene ambulances, emergency equipment, control van, canteen van, floodlight tender, and fire fighting equipment

At the scene the medical officer in charge of the casualty services, who will be a senior surgeon, will keep in close touch with the senior police officer and the senior fire and ambulance officer His duty will be the organisation and direction of all first aid services, including those offered by people who go to the accident on their own initiative He will advise the medical coördinating officer how many casualties there are likely to be and how things are going

At the control centre, the medical coordinating work in conjunction with representatives of the fire and ambulance service, the St John Ambula the Red Cross, the executive council, and the authorities to see that all the arrangements go best possible way

General practitioners and other doctors the scene within a few moments of the acci Birmingham authorities decided that it would put out hospital first aid teams in support consisting of 1 doctor and 4 nurses, are on imme hospitals in the area, and another 10 teams are two hours' call The plan sets out in detail the which the teams will take with them.

The blood transfusion service will be asked to squad, including specially trained personnel of the Ambulance Brigade and the British Red Cross industrial medical officer, if possible with a first a nearby factory, will also report to the incident

The clerk of the executive council will ask 3 tioners in the neighbourhood to help, and another themselves in readiness

The plan also includes details for mobilising the St John Ambulance Brigade and the British Red C

The hospitals themselves will arrange to sending home patients who are fit to go They coördinating officer at half hourly intervals, or if necessary, of the changes in their resources for outpatients and inpatients

This is the outline of a plan that is straightfo precise—the logical application of the m battle evacuation to a thickly populated area Sutton Coldfield accident it was never nece the whole organisation into top gear, but it that it could readily have handled the grav that might have arisen if the Birmingham had run into the wreckage—as so nearly was made plain at Harrow and Wealdstone years ago that any official plan can always flood of unofficial help from all around, and again forthcoming on this occasion Local pr nurses, and many others were quick to res valuable assistance came from a nearby R.A

### *Experiences at the Accident Hospital*

As for the details of the plan, the most c point is just how much in the way of resusc other treatment should be undertaken before are moved to hospital Last week Mr William clinical director of the Birmingham Accident discussed the outcome of the accident colleagues at the Accident Hospital, and one questions they considered was whether a m type of casualty-clearing station could be set site of a serious accident or whether speed was in fact the most important thing to con Mr Gissane and his staff thought that for a ma in Birmingham within, say, five to eight mil Accident Hospital, speed of evacuation to that should be the overriding consideration Once hospital full resuscitation and treatment be brought to bear If the journey to hospital wa miles there was, they felt, a case for setting up a clearing station at the site, although this ob many practical difficulties It would always be of considerable organising difficulty to set up casualty-clearing station at the site of an accide adequate medical control, with a speed in comparable to that of the rescue and ambulance Mr Gissane pointed out that to justify more on the spot it was necessary to establish the clearing station very quickly—say, within fort of the disaster And it was vital that a exceptional experience should be there to ass cases should wait and which should go on Another point to consider was whether the h which the injured were to go had a full emergenc go into action One of the men injured at dfield was in urgent need of resuscitation when the Accident Hospital at 5 15 P M (one hour rash) and the feeling was that this was a case ransfusion might profitably have been started t. The possibility of having specially trained to start transfusions was mentioned One atients might have travelled better if more had been applied. Mr Gissane said that first be simplified by the use of a new type of which was under investigation at the Accident This was made of fibre glass lined with foam l so moulded to the body outline that when the s placed in it the limbs were effectively splinted l movements reduced

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[1] See *Lancet* 1954, i 1225

point brought out at the discussion was the e of local knowledge things were much the surgeon in charge at the scene when he was y familiar with the district and with the e ambulance and fire personnel and others oncerned When it comes to supplying informa control centre the difficulty may be to estimate number of casualties which can never be easy injured are entangled in heavy wreckage. It may s be possible for those on the spot to say where ated casualties have gone to or how many have way Clearly if the injured are being extricated different places and taken off by various routes t always be feasible to give the control centre nbers without risk of delaying the ambulances cident Hospital received 13 of the casualties he same number as came in from other sources e same time Sutton Coldfield Cottage Hospital s very close to the accident took most of the the first place and acted as a casualty-clearing n the way to the big hospitals

*n or Resuscitation?*

eryone will agree that there is much of a case ng the removal of shocked patients so that their can be improved by giving plasma or blood s As we said after the Harrow accident[1] ople will think that in an area where big hospitals n easy reach it is better to get the injured away waiting to do more than cover open wounds, ctures, and give morphine and that the only ication for immediate transfusion or operation h seriously shocked person is trapped with little f being got out for some time It may be a matter when there is a long way to go or when by road is likely to be bad In these circum helicopters would be very useful All things d it seems it would be an exceptional accident— ountry at any rate—in which the injured once d, could not be got to hospital so quickly that delay for resuscitation or operation would be ed But that is not to say that arrangements ediate transfusion or surgery should not be in the plan they may rarely be needed but they save life

## NERAL PRACTICE IN SCOTLAND

ixth annual report of the Scottish Medical Committee[2] states that at the end of last ere were 2543 doctors undertaking to provide medical services in Scotland compared with 2505 and 2424 in 1952 As a result of the notional yments many doctors have taken partners for t time or in established partnerships, have d the number of partners For the first time start of the National Health Service the average number of patients on doctors' lists throughout Scotland has fallen below 2000

### ENTRY INTO PRACTICE

During the year 106 doctors died or resigned, and the committee granted 143 new applications for admission to medical lists Of these applications 43 were from doctors who had been selected to fill practice vacancies (including 13 to fill vacancies in partnerships) 82 from doctors who wished to enter into partnership with established doctors, and 18 from doctors who wished to set up new and independent practices In addition there were granted 64 applications from doctors already on medical lists who wished to extend their practices into neighbouring executive-council areas

The committee refused 26 applications for inclusion in lists of which 15 were from doctors wishing to extend their practices into neighbouring areas Of the 11 appeals to the Secretary of State for Scotland against these refusals 2 were withdrawn before a decision was reached in 8 the decision of the committee was upheld and in 1 the decision of the committee was modified 2 other doctors appealed against the imposition of conditions by the committee in granting their applications for admission. In both instances the decision of the committee was upheld

During the year practice vacancies were dealt with as follows

| | | |
|---|---|---|
| (a) Filled after advertisement | | |
| (i) by a doctor new to the area | 24 | |
| (ii) by a doctor already on the medical list for that area | 2 | |
| | — | 26 |
| (b) Filled without advertisement | | |
| (i) by the replacement of a partner | 13 | |
| (ii) by the appointment of a new doctor | 4 | |
| (iii) amalgamated with existing practice or practices | 29 | |
| | — | 46 |
| (c) Dispersed (patients advised to make a fresh choice of doctor) | | 23 |

Of the practices dealt with by amalgamation 6 had lists of under 500 patients and 11 lists of under 1000 All the dispersed practices were small the largest had 527 patients.

Over 800 applications were received for the 20 advertised vacancies. But some applicants applied for more than one vacancy The average age of successful applicants during the year was 30 the range of ages being from 27 to 56 Of the 13 appeals by unsuccessful applicants, 1 was withdrawn 9 were determined summarily; and 3 were decided after a hearing In 2 instances both after a hearing the decision of the executive council was overturned In the remainder the selection of the executive council was upheld When an appeal is successful the committee directs that the successful appellant be appointed instead of or in addition to the doctor selected by the executive council

### CERTIFICATES IN CONNECTION WITH GOODWILL

The committee considered 26 applications for a certificate that a proposed transaction did not involve unlawful sale or purchase of the goodwill of a practice Where the committee was at first unable to grant the desired certificate most of the applicants submitted amended proposals which justified a certificate The committee draws attention to the fact that the sale of goodwill is prohibited no matter how indirect that sale may be The performance of services for an unreasonably low return for instance is deemed to constitute the sale of goodwill whatever the intention of the parties may be The committee appreciates that difference in age experience and ability of the partners justifies some initial disparity in shares of the profits but as the new partner gains in experience and assumes a greater responsibility in the work of the practice his share in the returns should increase proportionately if the return for his services is to be regarded as reasonable

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embers of the ommittee are Dr A F Wilkie Millar, Walter Joll, Dr J R [illegible] Mr A I Millar, Stewart Sandeman and Mr H A [illegible] Q.C.

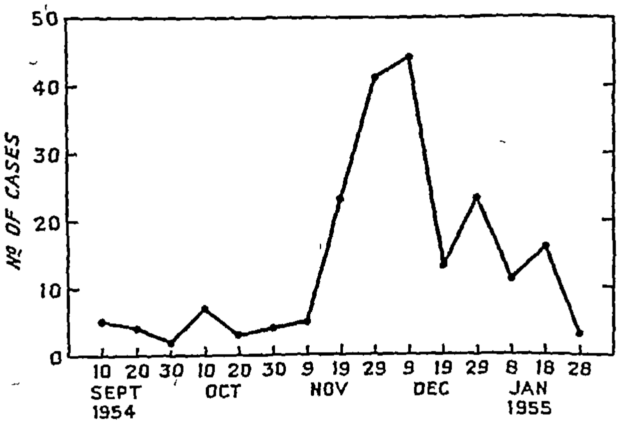
# Public Health

## INFLUENZA

This winter's influenza seems to have been mostly due, until now, to the B virus There were a few cases of influenza-B infection in the spring of 1954, and the virus was found in Wales in September, and then in the North of England, in Scotland, and, more recently, in the South of England The over all incidence in the country has not been so high as during epidemics of influenza A, all ages have been affected, but there has been a high attack-rate in children The last epidemic of influenza B of comparable size in this country was in 1945–46, since when the infection seems to have been endemic with sporadic cases detected each winter Presumably, therefore, the children infected this winter include many who escaped the 1945–46 epidemic

Influenza-A epidemics usually occur every *two to three* years, and in this country we had epidemics in 1947, 1949, 1951, and 1953 This year the influenza A virus has apparently defied the laws of arithmetic, and there have been *only sporadic cases* Elsewhere in the world there have been no reports of major epidemics of influenza An epidemic of influenza B was recently reported from Northern Holland, and cases have been notified from Germany, Malaya, and Canada The winter is not yet over, but in the world as a whole the contrast between this winter's experience so far and that of an epidemic winter is very striking

In England and Wales deaths attributed to influenza in the 160 Great Towns rose from 15 in the week ended Nov 13 to 66 in the week ended Dec 18 In the week ended Dec 25 the total was 56, and in the four weeks ended Jan 1, 8, 15, and 22 the numbers were 82, 102, 134, and 136



**Influenza in a Gloucestershire practice of 3485 patients: new cases plotted at 10-day intervals.**

The prevalence of the disease, which seems to have been greatest in November, has apparently varied between places quite close to each other

### *North of England*

A practitioner in a town near Darlington writes that there the disease was virtually confined to the month between mid-November and mid-December, but there have since been a few sporadic cases In the nearby towns of Darlington and Stockton-on-Tees an epidemic started in the first weeks of November, but in a small village three miles north of his practice there were very few cases, even though many of the adults work in one or other of these towns.

The epidemic, though short-lived, was the worst as regards number and severity, in the past seven years At first the infection affected principally those aged 5–10 years, and at one time the school attendance of those in this age group was only 33–38% of the total

Clinically there was sudden onset of feve sore throat, and sometimes cough, epistax mon, and in several cases this was profu In perhaps a quarter of the cases in ve pyrexia persisted *for five to seven* days, and c took two to three weeks About half the a were severely affected, with gross lassitu febrile phase Among the children the complications Among the adults complicatio pneumonia (4), otitis media (2), and arthriti

TABLE I—AGE DISTRIBUTION OF CASES OF CLIN IN A GLOUCESTERSHIRE PRACTICE, SEPT 1, 19 1955

| Age (yr ) | Male | | | Female | | |
|---|---|---|---|---|---|---|
| | Pop | Influenza | | Pop | Influenza | |
| | | No | % | | No | % |
| 0– 9 | 285 | 22 | 7 7 | 285 | 34 | 11 9 |
| 10–19 | 189 | 23 | 12 2 | 208 | 25 | 12·0 |
| 20–29 | 205 | 5 | 2 4 | 237 | 14 | 5 9 |
| 30–39 | 268 | 6 | 2 2 | 244 | 19 | 7 8 |
| 40–49 | 270 | 13 | 4 8 | 217 | 10 | 4 6 |
| 50–59 | 213 | 7 | 3 3 | 191 | 6 | 3 1 |
| 60–69 | 163 | 4 | 2 5 | 179 | 5 | 2 8 |
| 70–79 | 113 | 6 | 5 3 | 140 | 5 | 3 6 |
| 80–89 | 30 | 2 | 6 7 | 41 | 0 | 0 |
| 90–99 | 2 | 0 | 0 | 5 | 0 | 0 |
| Total | 1738 | 88 | 5 1 | 1747 | 118 | 6 8 |

### *West Country*

A doctor with a mixed urban and rural Devonshire writes

"Here the epidemic started in November b appears to have passed its peak The disease spread and highly infective, has been mild Se cations have been extremely rare Children s been affected more than adults In most case stage has not lasted longer than three or fou occasionally it has lasted for a week or more festations other than pyrexia have been headac sore throat, cough, and gastro intestinal distu colic, vomiting, and diarrhœa For quick rec bed has proved of paramount importance, with the aspirin group for the relief of symptoms. C pyrexia has been prolonged have apparently re aureomycin"

From Gloucestershire a doctor with an rural practice of 3485 patients reports tha Sept 1 and Jan 24 there were 206 cases o influenza" (This he defines as a febrile illness onset, associated with aching and upper r infection) There was a small burst of cases in and a much more severe one in November and with a peak in the ten days between Nov 1 (see accompanying figure) The figures for include an explosive outbreak affecting chil 14 years of age, in whom the syndrome includ severe pyrexia, delirium, and epistaxis One red vision "She saw the world literally re for a few days before the onset of fever" Co have been few, the two commonest were oti

TABLE II—AGE DISTRIBUTION OF THOSE ATTAC INFLUENZA BETWEEN SEPT 1 AND JAN 7 IN 1 295 VOLUNTEERS

| Age (yr ) | Males | Females |
|---|---|---|
| 0– 9 | 23 | 19 |
| 10–19 | 8 | 8 |
| 20–29 | 1 | 7 |
| 30–39 | 8 | 12 |
| 40–49 | 8 | 3 |
| 50–59 | 1 | 5 |
| 60–69 | 2 | 3 |
| 70–79 | 1 | 1 |
| 80–89 | 0 | 0 |
| Total | 50 | 58 |

* 36 6% of total

ionia (10) ,4 patients had a second attack ;
patients who for the past twelve months have
ng a daily record of the presence or absence
ry illness, 10 recorded second attacks Tables
w the age and sex distribution of cases in the
d in these volunteers. The incidence is clearly
he volunteers and the difference may give
ide to the proportion of patients with illness
who do not seek medical advice. So far the
been neither so common nor so severe as in
of 1951 and 1953

*ties and London*

tioner in Buckinghamshire writes

a reached us about the middle of January and
cond of Jan. 22 the epidemic was at its peak it
on the wane now The virus afflicts all age groups
tively mild there have been no deaths It is
tious whole families being affected the housewife
or feet until her family is over the worst, then
erself Three quarters of the school-children were
ce.

ubation period is about three days the onset is
y feelings and sore throat followed by headache
in the back and limbs. In this epidemic aches and
metimes distressingly severe but often are absent
ation occurs with little discharge and an irritating
lops A few patients have abdominal pain and
This melancholy business drags on for four or five
ng the victim weak and depressed Otitis media
n occasional complication

itioner in North London doubts whether he
this winter any cases of true influenza and
here has been no epidemic among his patients
s seen sporadic cases of a febrile illness starting
ro-intestinal disturbance (abdominal pain or
This clears up in twenty four hours ; there-
exia persists for three or four days, but the
oes not fully recover for a further seven to ten

## Medicine and the Law

### A Doctor's Telephone

ndon Executive Council has ruled that a doctor
quired to have a telephone at his residence or
nd that if he has a telephone he is not obliged
patients use the number [1]

ling was given on a complaint by a mother who said
aited all day for the doctor to visit *her 8 year-old*
who had tonsillitis She could not get in touch with
r because as far as she knew he was not on the
She could not go to the surgery because there was
look after the child When her husband arrived home
ning they found another doctor—who treated the
private patient

dical services committee held an inquiry In its
the council it said that the first doctor admitted that
telephone but said it was not available for patients.
mittee considered that there had not been a breach
nditions of service The members of the council
approved of the doctor's conduct, but adopted the
dation that he had not committed a breach of the
service A member of the council suggested that the
ould insist on going on the list of a doctor who was
by telephone

uncil's ruling is clearly correct having regard to
s of service attached to the General Medical and
eutical Services Regulations But these statu
ms of service which must be incorporated in
dividual contract are not exclusive The execu
ncil is entitled to add to them and this can be
en after the contract has been entered into
l the Minister of Health gives his sanction

### Postal Treatment

harmacy and Medicines Act 1941 makes it an
o sell in retail any articles consisting of a substance recommended as a medicine without the appropriate designation or quantitative particulars This does not apply to an article made up and supplied for the use of a particular person being an article prescribed by reference to the needs of that person This exception is essential—without it no chemist could make up a doctor's prescription—but it provides a loophole for firms who claim to treat diseases by post

Mr H H Bagnall the city analyst of Birmingham in his report for the third quarter of 1954 mentions the case of a firm who claimed to treat psoriasis in this way In one case the firm supplied a medicine containing a common purgative an ointment which was an emollient cream containing lanolin and a powder to be used for making a lotion this last item consisted of boric acid

Mr Bagnall suggests that the law should be amended to require that all stock mixtures powders pills and so on should be labelled with a list of ingredients unless they are supplied on prescription by a doctor

## Parliament

### Care of the Elderly Sick

In the House of Commons on Jan 28 Mr HECTOR HUGHES drew attention to the inadequate provision made for the elderly sick The problem, he declared presented a striking paradox. Hospital accommodation would be adequate quantitatively at least, in most areas if local authorities developed their preventive and domiciliary services to the full As a result with some exceptions the regional hospital boards were unwilling to increase the number of beds for the elderly Many local authorities instead of putting their own house in order blamed the regional hospital boards for not providing more beds An important contribution to the problem in his view would be to bring the full number of health visitors into operation Their salaries, pensions, and general conditions should be improved to encourage recruiting Old people must be kept out of hospital as far as possible and that was where the health visitor was the key The present scarcity of health visitors placed unduly heavy case-loads on the comparatively few Before 1918 when health visitors were concerned only with expectant and nursing mothers and young children the standard case-load was 100 to 120 births per health visitor per year With a normal birth-rate of 16 to 17 per 1000 of the population that meant that before 1918 a health visitor was needed for every 6000 to 6500 of the total population Today with her extended duties, it was impossible for the health visitor to cover a population of more than 3000 and many experts advocated smaller case-loads

Mr SOMERVILLE HASTINGS thought that the first thing to do was to improve the services for finding out when old people—and particularly those living alone—were ill and needed help In many areas there were preventive clinics for old people which provided means of keeping in touch with these cases. He agreed that old people should be kept out of hospital as far as possible They often seemed to die there from some inexplicable cause Like other people if they were to be healthy they must be kept busy He would like to see more one-storey flats built in housing estates so that elderly people could avoid stairs. Though it might cost local authorities money to treat old people in their own homes it was infinitely cheaper to the community than removing them to an expensive hospital quite apart from the additional happiness to the patient.

### QUESTION TIME

### Air Pollution

Replying to a question Mr DUNCAN SANDYS Minister of Housing and Local Government said that the main recommendations of the Beaver Committee were as follows

(1) That subject to certain exceptions the emission of dark smoke should be prohibited by law

(2) That industries when installing new plant should be required to take all practical steps to prevent the emission of grit and dust

(3) That subject to confirmation by the Government, local authorities should be empowered to designate "Smokeless Zones" and "Smoke Control Areas"

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[1] *Daily Telegraph* Jan 28 1955

(4) That the duty of inspection and enforcement should be placed upon local authorities except in the case of certain industrial processes, which should be supervised by Government inspectors

(5) That householders in smoke restricted districts should be required to burn only smokeless fuel and that the cost of converting domestic fireplaces for this purpose should be met, to a large extent, by grants from the Exchequer and the local authorities

Mr Sandys said that the Government were examining with outside interests the far reaching questions involved Preliminary discussions indicated that industry would be ready to play its part in implementing this policy, and that the local authorities would be prepared to accept the additional responsibilities involved Similar consultations were taking place in Scotland The Minister of Fuel and Power was examining the question of increasing the availability of smokeless fuels While reserving their position regarding individual proposals, the Government had decided in principle to adopt the policy recommended by the Beaver Committee

### Training of Spastics

Replying to a question, Mr H A. WATKINSON, parliamentary secretary to the Ministry of Labour, said that he was aware that some spastics at school-leaving age or later might profit from a course of preliminary training before employment, to enable them to use their limbs more effectively He understood that the voluntary organisations had in mind the establishment of centres where this kind of training could be given One of the voluntary organisations had discussed it with officers of the Ministry of Labour and was aware of the extent of the assistance which could be given at a later stage of training under the Disabled Persons (Employment) Act

Mr E S T JOHNSON Is the Minister aware that the existing centres cater chiefly for lightly handicapped spastics and the hard core of the problem of employment and training of spastics is not really touched ?—Mr WATKINSON It is hoped that, as a result of the initiative of the bodies interested, there will be further centres, and, if so, we shall do what we can to help

### Patients' Diet

Replying to a question, Mr IAIN MACLEOD, Minister of Health, said that he was informed that since July, 1953, the Dartford Hospital Management Committee had authorised the officers in the general hospitals in their area to spend up to a certain weekly sum per head of staff and patients without further reference to the committee The sum was at present 26s a week There was no such procedure in the mental hospitals in the area

### The Case of Mrs Christofi

Replying to a question, Major GWILYM LLOYD GEORGE, the Home Secretary, said that of the three doctors appointed to conduct a medical inquiry into Mrs Christofi's mental condition, one held a diploma in psychological medicine, and the other two—a former medical superintendent of Broadmoor Institution and a former director of prison medical services—had long and special experience of cases of this kind The doctors had two prolonged interviews with the prisoner They also interviewed the governor of the prison, the Church of England chaplain, the prison medical officers, the Greek Orthodox priest who ministered to Mrs Christofi, and the prison officers who had charge of her

### Medical Superintendents of Mental Hospitals

Mr KENNETH ROBINSON asked the Minister of Health if he was now prepared to make a statement on the observations of the Central Health Services Council with regard to medical superintendents of mental hospitals —Miss PATRICIA HORNSBY SMITH replied The Minister does not consider that it would be appropriate at present to introduce model standing orders for the general government of mental and mental deficiency hospitals defining the functions of the medical superintendent

### Cost of Proprietary Medicines

Replying to a question, Miss HORNSBY SMITH said that discussions had been proceeding with the Association of British Pharmaceutical Industry, and the Minister of Health was considering the position now reached Meanwhile, there had been some downward trend in the prices of preparations in those classes which were under investigation, and special provisional reductions had recently been arranged with certain manufacturers in the prices of 19 of these preparations

# In England Now

*A Running Commentary by Peripatetic C*

IT was a bitterly cold day early last m set out to visit the Blanks There were fo Welfare Worker, the Farmer, the Clerk to t and the Medical Officer of Health (me)

Mr and Mrs Blank, aged 84 and 79, th within seventy miles of London, live in a spot To reach them you go up a side- then along a rough cart-track for a mile that even the farm-truck can go no further out and walk. After crossing four fields you cottage Nothing is ever delivered to su the-way place, no milk, no coal, no paraffin has to be carried by Mr Blank from the which is several miles away For fuel he from a nearby coppice In winter the wet and will only smoulder It is practically for them to prepare any hot food Mrs. Bla crippled and hobbles about with a stick. been away from the cottage for eight years.

Many attempts have been made to persuad to move to an old peoples' hostel or home, b always refused During the past few month had clearly worsened, and we were all w what could be done to help the old coup impossible to send a home help to a place beaten track, because it takes most of a make the journey For this reason, too, Worker could not visit them often. So Farmer's wife prepared some food and took long journey to the cottage, but she was and could not do this often

So we all set off on this cold winter try once again to persuade the Blanks to go and, if we were not successful, to consider pulsory removal under the National A I was anxious to avoid this For one thing I pushing people around, and for another I that a compulsory removal across four present technical difficulties

The old man opened the cottage door in our knock The furniture consisted of a chairs, and a cupboard which Mr Blank was to get some dry wood for the fire Dirt a cobwebs were everywhere Mrs Blank sat the grate, where one ember glowed fitfully on was a threadbare dress and an old coat were poking out of an ancient pair of shoes places The old people had had nothing to e and there was no food in the house. Mrs. Bla to think that it would be rather nice to go where she could be warm and comfortable was sure that he didn't want to move We talked and talked, but we were up against Any members of the party not engaged gathered sticks and tried to make the fire Mr Blank refused Still we talked on Th he relented and said he would like to accept

We set off across the fields to the farm got busy with the telephone We must have tion at once, we said, we must have it toda that another night in the cottage might m of Mrs Blank The welfare services rose situation A vacancy was found and soon car was on its way The Farmer solved the how to convey Mrs Blank across the fields, a tractor standing by with its trailer padded bales of straw This could go right to the co A strange procession then began to wind its the fields, tractor and trailer, followed warily car, followed by the farm truck. When the as far as it dared we all dismounted and tractor on foot We wondered if Mr Blank have changed his mind and refuse to com but all was well Mrs Blank was assisted to where she reclined in the straw and we sur with hot-water bottles and covered her with Mr Blank got in beside her, and we, bec journey back The temperature was round and it was Mrs Blank's first journey for

have been worse, said the Welfare Worker
have been raining ' By the time we reached
rs. Blank didn't look in very good shape
ve were only just in time said the Farmer
tucked up in the car with a hot drink inside
Blank soon revived " It is very kind of you
Blank, " to help us in this way very kind
went to the car to have a last look to see that
ll with his wife before the next stage of the
Are you feeling comfortable ? I asked
warm she assured me; and her dirt-grimed
d as she added ' what I m really looking
more than *anything* is a nice hot bath

* * *

e I can help my fellow peripatetic in his
over the draught proofing of his cat hole
of hard board should be pivoted at the bottom
rio or leather hinge such as is found on clothes
condly the base of the flap should be increased in
o that of the door by nailing a piece of square
ng each side of the hard board Two pieces of
tic stretched one from each side of the flap to
he door below the hole will then cause the flap to
to the shut position after the animal has passed
t will remain closed even in strong wind

n hole was made for a cat, and afterwards
or a Shetland collie We have now moved
I believe the new owner (a dachshund) uses
difficulty
o your correspondent s puppy objects to using
nd forehead to raise the flap With our modifi
s forefoot is used to depress the flap and hold
I tried fitting a piece of door-mat to the outer
e flap in order to reduce the incidence of foot-
the kitchen but my wife reported that the
not statistically significant. At her insistance
s fitted giving control of the inward opening
)

* * *

obile antenatal and child welfare clinic was
n *from my district of darker Africa* because
e was inadequate. But the following letter
hat we underestimated its place in the public

seems apparently clear that for some months now
Van of your department has seized plying her way
e various towns and villages she used to visit
as you are well aware of bestows a lot of health
idance and innumerable series of help on depressed
nd old infirm elements in her course of travel
very well picture out the dreadful conditions into
natives concerned are thrown these days of her
work
herefore by request to solicit your favour earnestly
r this awful situation of our people and let the Van
h her beautiful piece of work should nothing so much
ur voice and decision

I have &c
Clerk of District Council

* * *

uch red tape necessary ? Defending its use a
vant once asked me : In what better way could
together say, several folders of papers some
phs and a book all on one subject ? An even
e for it was revealed to me yesterday on a
a Ministry (not Health) Sitting with a desk
me and my host, I noticed that my chair lacked
on inspection I discovered it to be attached to the
h red tape and pins. This device apparently
ts borrowing

* * *

ntious *New Assistant* There s a call just come
o go and see Mrs. X.
*al* Oh well that could probably wait till tomorrow
*l* Well it might be urgent
onsense I know Mrs X. If it couldn t wait till
she would have phoned yesterday

# Letters to the Editor

## AN ISONIAZID DERIVATIVE

SIR —We have previously outlined the tuberculostatic properties of *o* hydroxybenzal isonicotinyl hydrazone and mentioned work on the effect of this new compound on the emergence of resistance to isoniazid.[1]

We have now shown that after eight transfers the minimum inhibitory concentration of isoniazid in vitro against *Mycobacterium tuberculosis* H37Rv increases from 0·03 µg per ml to 81 µg per ml. while that of *o* hydroxybenzal isonicotinyl hydrazone ( Nupasal 213 ) increases from 0·06 µg per ml to 7 81 µg per ml Thus the resistance to these two drugs separately is increased 260 and 130 times respectively On the other hand in mixtures of the two substances, isoniazid at a constant level of 0·01 µg per ml has allowed the resistance to nupasal to develop from 0·06 µg per ml to 0·48 µg per ml —that is an increase of only eight times—even after ten transfers Similarly a constant level of 0·01 µg per ml of nupasal has permitted an increase in resistance to isoniazid of 0·03 µg per ml to 0 24 µg per ml.—again only an increase of eight times—in ten transfers.

Thus isoniazid and *o* hydroxybenzal isonicotinyl hydrazone appear to act mutually on the development of resistance each drug distinctly delaying the *emergence* of resistance to the other

This result appeared at first somewhat surprising in view of the close chemical relationship between the two drugs but our findings have been confirmed by Steenken et al[2] These results suggest that the combination of isoniazid and nupasal 213 may be of clinical value in *delaying emergence of resistance to both substances and* experiments are now in progress to obtain further evidence on this point

Smith & Nephew Research Ltd
Ware Herts

E M BAVIN
F KAY
D F SEYMOUR

## *VENEREOLOGY AND DERMATOLOGY*

SIR —I have followed the correspondence on this subject with dismay as I have learnt from it that there is a tendency in some quarters to relegate the care of venereal diseases to dermatologists as in the bad old days when in the infancy of the national venereal disease service under the Local Government (Venereal Diseases) Regulations, 1916 hospitals asked to establish venereal-disease treatment centres within their walls almost automatically handed the charge of them to their dermatologists or much less often to their urologists In twenty seven years as adviser on venereal diseases to the Ministry of Health I had ample opportunities of judging the weaknesses of such an arrangement and have no hesitation in saying that the principle is bad Whatever may be the practice in other countries neither the dermatologists nor the urologists in this country have generally speaking been really interested in the management of venereal diseases in all their aspects—scientific diagnosis far-seeing treatment and epidemiological control—and I count amongst the few good things I have done in my life the divorce of venereology from dermatology which I began at Rochester Row in 1910 Today the combination of dermatology with venereology is even less supportable than it has ever been because to judge by the annual report of the chief medical officer Ministry of Health for the year 1953 of the 98 671 new cases dealt with by the venereal-diseases treatment centres in England and Wales in that year only 6512 were of syphilis or soft chancre I do not know how any venereal disease came to be regarded as within the province of dermatology but assume that it was because a common feature of syphilis now relatively uncommon

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1 Bavin E M., Kay D., Seymour D E. *Lancet*, 1954 ii 33
2. Steenken, W , Wolinsky E Montalbine V *Proc Soc exp. Biol.*, N Y 1954 87 245

was a rather persistent rash As regards the remaining fourteen-fifteenths of the new cases seen in the centres in 1953, one would judge that, in the absence of trained venereologists, their management would more appropriately be entrusted to the urologists and the gynæcologists

Admittedly there may not be work in many centres to require a visit by a consultant venereologist even so seldom as once a week, but it should be easy to train medical men and women of less than consultant status to carry out instructions, given at appropriately spaced visits, by consultant venereologists It is in diagnosis and the framing of instructions for treatment and the prevention of transmission of venereal diseases that the skilled venereologist is required, and if this work is relegated to dermatologists, whose chief interest is rightly in another sphere, great harm will certainly result The management of venereal diseases may seem simple to the administrators who arrange the manning of the different medical services, but I feel sure that such a view would change if they visited a well conducted venereal-diseases treatment centre They would see that the good venereologist, besides making good diagnoses and arranging good treatment, must do all those things which have for their object not merely the prevention of transmission of venereal disease by the patients before them but the prevention of further transmission by those responsible for their present patients' infections Thanks to the antibiotics, a very useful step forward has been made in the campaign against the venereal diseases, but the battle has not yet been won, and to act on the assumption that the remaining problems are negligible is to risk the loss of valuable ground, as a study of table A in appendix C of the C M O 's annual report already quoted would show

London, S W 1 L W HARRISON

## NEW STUDENT UNIT AT HIGH WOOD HOSPITAL

SIR,—The British Student Tuberculosis Foundation in cooperation with the North West Metropolitan Regional Hospital Board, has been administering a "pilot" rehabilitation unit at Pinewood since September, 1952 Here, men students from all parts of the British Isles can gradually resume their studies under medical supervision until they are fit enough to return to a full college life Arrangements have now been completed for the establishment of a further unit, at High Wood Hospital, which will cater for women students needing active treatment for tuberculosis This broadens the scope of our services, hitherto confined to men in the convalescent stage These two units will meet the needs of the tuberculous student until the foundation can open a single permanent centre capable of fulfilling the demands of both men and women students from all over the British Isles

The North East Metropolitan Regional Hospital Board will open a small unit in Brentwood Hospital Management Committee Group at High Wood Hospital, Brentwood, Essex (senior physician, Dr F J Bentley) Here women students from all parts of the British Isles may undergo treatment right from the detection of the disease until convalescence is completed High Wood Hospital is on the outskirts of Brentwood Being less than half an hour from Liverpool Street by frequent trains, it is conveniently near London University The hospital has always been devoted solely to the care of tuberculosis in children and young people, one of the few such specialist hospitals in the country, and its patients have always been drawn from a large area, coming from places as far afield as Southampton and the Isle of Wight in the south and Harwich and Bedford in the north In the hospital there is a permanent school with some 17 teachers There are always about 30 children of grammar school standard and some of these girls will occupy the parts adjoining the accommodation for women students The long established educational atmosphere, friendly but serious, will be a help to women students in continuing their studies as they become fit to do so The ward chosen is pleasantly situa [illegible] midst of trees and rural surroundings Each bed is supplied with relay wireless system wi and a choice of programme Television and general amenities will be available

The medical care and maintenance of stud the new unit have been accepted, as at Pin hospital board, under the terms of the N Service, and no fees will be chargeable

Academic arrangements, as permitted by t authorities, will be administered under the sup foundation's academic subcommittee, and no chargeable to students for the study facilities main bulk of teaching will be given by visiting teachers, who will supervise the students' w correct written work, and guide reading The itself possesses a small library of standard te book requirements can be met from this and oth

All applications will be considered first by the subcommittee, which will then forward its re tions to the medical authorities Applicatio be obtained on request from the secretary of the foundation at 59, Gloucester Pl Square, London, W 1

NICOLAS
Hon.

## CHLORPROMAZINE AND GASTRO

SIR,—For many years it has been my perform gastroscopy on outpatients, who hospital in the morning, have the examin early afternoon, and return to their homes evening All have felt nauseated to some ex the examination, most of them also suffered and about 1 in 10 have had to be retained in ho night because of persistent vomiting My la have been given 25 mg of chlorpromazine by muscular injection immediately after gast these 50 only 4 have had any nausea ( 3 by retching), while none have had to be r hospital 3 had painful injection sites cl taneously after seventy two hours It seems t chlorpromazine is well worth using as a rout gastroscopic examinations I am indebted t house-physician, Dr D J Gorham, for kind these records

London, W 1 A MO

## SULPHONAMIDE SENSITIVITY OR L ERYTHEMATOSUS?

SIR,—I read with interest the case of sul sensitivity reported by Dr Fox in your issue o While not doubting the diagnosis in this case I certain comments should be made

Firstly, sensitivity to drugs may be seen at during their administration, often after amounts have been taken It should not b with toxicity, which depends upon total d the present case, therefore, it is not the eruption occurred with sulphadimidine comparatively small total dose

Secondly, the statement that "the diagnos erythematosus was excluded by the marrow seems to imply that a negative L E -cell te lupus erythematosus Although in many of and subacute disseminated cases L E cells ma either in bone marrow preparations or in the blood, negative tests are by no means unknown wise typical cases Furthermore, it appears tha tion for these cells was only carried out on o A single negative test should not be accepted the presence of these cells, and in suspicious test should be repeated on a number of occasio

Thirdly, hair fall may be common in sul sensitivity, but also frequently occurs after a febrile illness and it would seem that the h this case might well be related to this rather th specific sensitisation to sulphadimidine

London, N W 6 R H Y

## "EPIDEMIC VERTIGO"

Leishman (Jan 20) describes a syndrome d by vertigo and some of the following innitus nystagmus and ocular paresis head omiting He thinks that this syndrome may en noticed in this country before and he adds people would not readily concede that the as due to an encephalitis

Dr R I Poston, of Manchester described[1] amns six cases of epidemic encephalitis which predominantly as vertigo with perhaps spon induced nystagmus There was a graduation usual picture of epidemic encephalitis with e palsies increased salivation respiratory c Dr Leishman says that on the Continent oidemic vertigo were sometimes accompanied epidemic hiccups were reported at the same epidemic of encephalitis in Great Britain in

one should hesitate before accepting Dr syndrome as being in any sense a new one must be grateful to him for reporting these e likes to think that these cases and those rred in 1952 will be carefully followed up over n to twenty years

J A R BICKFORD

## SANATORIA

your leading article of Dec 25 prompted by of the Trudeau Sanatorium you questioned he value of the sanatorium treatment of Mr L J Temple (Jan 8) has leapt to the sanatoria but we cannot find ourselves wholly ent with him

ny years it has been a heresy to suggest that is could be adequately treated anywhere but torium However in 1946 when a waiting a year for admission was not unusual many ysicians undertook domiciliary treatment of us patients and attempted to bring the sana gime to the home. In some areas minor collapse (artificial pneumothorax pneumoperitoneum rush) were added to the routine of rest and l exercise In Southwark the results appeared re not unfavourably with the published results rium treatment in fact, not a few patients had to work before a sanatorium vacancy had been Domiciliary treatment at first much frowned appears to be generally accepted

lvent of the new antibiotics has revolutionised ment of tuberculosis It is common to see on bed rest and chemotherapy improve as much as it would have taken months or years on rium treatment alone This observation has us to try ambulant chemotherapy in patients rly diagnosed lesions of doubtful activity and others with older lesions showing a tendency to spread We had not intended to publish our ntil we were able to give impressive figures with able follow up period as we wished to have an o the storm of abuse which we expected As ding article however has tentatively suggested t chemotherapy we would like to report that lts so far are highly encouraging We are of the that the relief which a patient feels when he is need not stop work is more conducive to a satis mental state than months of watching the uty of forest and meadow from a sanatorium We encountered some difficulty with one who had received his education in a very strict um We are glad to say he is getting better against his better judgment!

We are of the opinion that it is possible to treat carefully chosen cases of tuberculosis with chemotherapy without bed rest We would remind your correspondents that the Guy's chemotherapy trials[1] are being carried out almost entirely on the ambulant chronic and their results are more than satisfactory having regard to the type of patient treated This series alone gives the lie to the axiom that a patient ill enough to be treated with antibiotics is ill enough to be in bed

Nor can we take the statement about self treated working medical practitioners very seriously A report on children's footwear based on a study of boot maker's bairns" would be equally misleading

In conclusion we feel that prolonged sanatorium treatment per se is necessary for a decreasing proportion of tuberculous patients, and that good results from chemotherapy in ambulant patients can be obtained in carefully chosen cases

Southwark Chest Clinic
Walworth Road S E 17

E K PRITCHARD
W E D MOORE

## OSTEO-ARTHRITIS OF LUSCHKA JOINTS

SIR,—Professor Cave and his colleagues are to be congratulated on their excellent paper (Jan 22) We should be grateful for their timely correction of the present tendency to attribute almost every case of pain in the neck or arm to cervical-disc protrusion

It is surprising that they found so low an incidence of related zygapophyseal arthritis in view of its common association with lumbar-disc degeneration The explanation must be that the Luschka joints protect the zygapophyseal joints I cannot agree that zygapophyseal arthritis is symptomless A zygapophyseal joint is diarthrodial and presumably responds to osteo arthritic changes like any other diarthrodial joint by synovial and capsular thickening which might well cause root irritation The posterior capsular ligament of a Luschka joint may be similarly affected Is it not therefore likely that the periarticular thickenings are responsible for many of the symptoms and that reversal of this process may lead to amelioration of the pain?

My main criticism concerns their statement that neck traction is valueless and is likely to aggravate symptoms My experience is exactly the reverse provided the technique is correct relief almost always follows

London W 1

F J CHISP

SIR —The interesting article in your issue of Jan 22 by Professor Cave and his colleagues makes it clear that resection of Luschka's neurocentral apophyses affords the only means of permanent cure for the cervical pains he describes They suggest however that such an operation may not yet be practicable when a number of these apophyses are involved

It so happens that their exposure is incidental to an operation for tying the reach of vertebral artery that lies between the transverse processes of the 3rd and of the 6th cervical vertebra This procedure forms a downward prolongation of the exposure of the topmost segment of the second stage of the vertebral artery (that between axis and atlas) which I described in 1927[2]

I have just received proof from my publishers of an account of this downward extension which will appear shortly in a new edition of *Extensile Exposure* I am indebted to Professor Cave for the opportunity of enlarging the scope of this operation for apart from its use in the late war by Colonel D C Elkin of the U S Army Service and nearer home by Mr Harvey

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[1] Poston R I *Lancet* 1927 i 438

[1] Joiner C L, MacLean K S, Pritchard E K, Anderson K, Collard P, King M B, Knox R. *Lancet* 1952 ii 813 Joiner C L, MacLean K S, Carroll J D, Marsh K, Collard P, Knox R. *Ibid* 1954 ii 663

[2] Henry A K. Exposure of Long Bones and Other Surgical Methods. Bristol, 1927

Jackson, it has had small currency lesions of the vertebral artery are rare in themselves and seldom reach base if they occur

Schools of Surgery
Royal College of Surgeons in Ireland,
Dublin ARNOLD K HENRY

## HEAT TO THE HEART

SIR,—Prior to the late war, I gave courses of short-wave diathermy to about a score of sufferers from coronary ischæmia, applying the heat over the heart area The majority were patients with angina of effort or angina decubitus, but a few had had coronary thromboses In such a small and uncontrolled series, and because I did not withhold other therapeutic measures, it was impossible to assess with any accuracy the influence of such treatment, but clinically most of the patients remarked an improvement in their condition and a diminution in the number of anginal attacks Nor were any ill effects observed, which, in these days of powerful dilators, hypotensives, ganglion blocking agents, ion-exchange resins, and anticoagulants, is perhaps some thing

London, W 1 S CHARLES LEWSEN

## "TAKE A COUPLE OF FAT VIPERS"

SIR,—If any compounder does not make use of the entrails and viscera of his vipers or if he has a surplus of these useful creatures (alive or dead) I shall be glad to receive them They should be used soon after death Decay is rapid and its results offensive

Public Health Laboratory
Musgrove Park Hospital,
Taunton J A BOYCOTT

## A WORD WANTED

SIR,—With regard to this discussion,[1] I suggest that, if we do not accept the word "prospective," on the ground that it is now used in a rather different sense to the one we want, we borrow from the Greek language the corresponding word, which is in everyday use That word is προοπτικός = prooptic It means "I see from the beginning the future evolution and happenings" A gifted politician is προοπτικός (a), a good clinician has προοπτική (n), and a good researcher must be prooptic and not retrospective only

Toronto, Ontario Canada L G POLYMENAKOS

## CANCER OF THE LARYNX

SIR,—I am well aware that the figures quoted from the Registrar-General's statistics cannot be regarded as altogether accurate, and I know that it is impossible to make allowances for the results of successful treatment when one studies these figures It would be most interesting to have the views of throat surgeons on this point, for it might convey some sort of idea concerning the degree of inaccuracy which arises from neglect to allow for successfully treated cases

I do not agree that the Registrar General's figures for death from cancer of the lung accurately reflect its incidence, as Mr Beales suggests in his letter last week The condition is still a most difficult one from the diagnostic point of view, and I should estimate that there is still a considerable percentage of error in the figures quoted One can only say that this error is much less than it was thirty years ago

Even if improvement in treatment has resulted in a masking of the true figures of carcinoma of the larynx, I feel that there is still a considerable discrepancy for which I cannot find a satisfactory explanation

London W 1 JAMES MAXWELL

## TOO MANY ANTIPYRETICS

SIR,—I use antipyretics in many because they seem to have a beneficial effect Fever produces symptoms, and minor febrile illnesses can only be treated cally and often this is all that is required.

Dr Bronsdon (Jan 29) says "On occasion I have allowed my own pyrexia the invading pathogens and it has coped It is Dr Bronsdon's antibodies that infection, not the pyrexia Furthermore, reason to suppose that the production of interfered with by lowering the pyretics (in fact there is evidence for the

The most reasonable view is that fever depression of sensitivity of the thermoregula by circulating toxins, and that this reaction of the host to the parasite value In addition, I do not think that can be increased by interpreting the febri teleologically

Finally, if it can be shown that patients antipyretics take significantly longer to those allowed to enjoy their fever unabated will be important evidence for those who elevated temperature is beneficial Meanwhi of antipyretics is rational as symptomatic

London S.E 2 PETER H

## VICARIOUS APPETITE

SIR,—Vicarious appetite is seen most behaviour disorder in children, during in various psychotic states I have lately patients with this complaint

CASE 1—A young Italian man, aged 27, the manager of a café, developed an insatiable desire in May, 1949 Simultaneously he lost interest food, and for *four months before* admission to ate literally nothing else He had no dyspep other symptoms being lethargy and a little los He estimated that he ate about three pounds per day during this time, his occupation allow privilege despite rationing He was examined patient at another hospital in June, 1949, and function" was diagnosed In August, 1949, he exhausted and was admitted to this hospital. his appetite, even for chocolate, was beginning to

He was a well nourished young man, compl a loss of energy and an inordinate desire to Physical examination of respiratory, cardiovascu urinary, and central nervous systems was complete A small hard movable mass was found in the Radiography after a barium meal confirmed the a gastric neoplasm At laparotomy this was inoperable, and he died two months later of

There can be little doubt that this vicario was based on the presence of a gastric

CASE 2—A girl, aged 6, with no previous histor attended the outpatient department of this January, 1953 The complaints were principally mother, and their vehemence was not surprising previously the child had started to eat her own appetite for more civilised foods remained norma the mother could judge, but in addition she ate dresses, gloves, &c An average meal consisted a square foot of convenient clothing A coat showing both sleeves eaten to the elbows and the up to pocket level The mother was in no doubt cloth being actually swallowed and not simply spat out She had noticed on several occasions a red coat in the child's fæces.

The child looked healthy She agreed that eat her clothes but would add little else Physical tion was negative She was charming and inte good at school, and she had never shown any disorder previously Her parents were kindly

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[1] See *Lancet* 1954 i 784 884, 1244 *Ibid* 1954 ii 759, 974 1020, 1179 1235 1286 1328 *Ibid* Jan 1 1955 p 48

in happy domestic circumstances until the
aval. Six months previously a second child
rn and the parents, together with the family
come to the conclusion that the clothes-eating
of exhibitionism based on jealousy of the newly
I rapidly joined their group and referred the
ychiatrist.
iths later I was again asked to see the child
ad been singularly unrewarding if not downright
From eating clothes the child had graduated to
ies, paper sticks, and coal The logical grouping
articles of diet gave me an uneasy feeling that
wing out clues to some deep-seated psychological
nature of which was quite beyond me She
s before in perfect health There was no
vomiting and no other symptom of alimentary

its were at their wits end The child was by
acceptable at school because of the habits she
ught others with latent similar appetites In
wardrobe was deplorable
nonth after this unhelpful consultation I heard
lady describe similar symptoms in a litter of
s. In her mind there was no shadow of doubt
cause—they needed worming I wrote to the
r and suggested that perhaps he might see whether
readworm infestation This he did and she had.

ed her carefully and in a few weeks she was
ling more abnormal than green iced cakes
gum.

Hospital,
anarkshire　A MUIR.

## TAL HEALTH AND PUBLIC HEALTH

Cameron writing in your issue of Jan 20
hat the health visitor is by her vocation and
ing as a sick nurse in general wards quite
or the tasks of working in the mental health

l like to ask him if the nurse why not the
s there any medical psychiatrist who prior to
on has not had similar experiences of the sick
wards to the nurses—or does he prefer the
al psychiatrist ?
of of the pudding is in the eating and in Cardiff
years now they have had a health visitor
g in mental health— Care and After Care
as liaison officer between the mental health
he general practitioners and the Cardiff city
itors all of whom are also interested in mental
The whole scheme works to the entire satis-
the Cardiff psychiatrists who also gave it
approval

J GREENWOOD WILSON
Medical Officer of Health, Port of London
formerly Medical Officer of Health,
City and Port of Cardiff

E.C 2

llow me to support Dr Cameron's plea for
into the problems of prevention of mental
e are not likely to get far with measures of
n until we know something more concerning
s of mental illness What are the causes of
enic diseases, which occupy nearly half of the
mental hospitals ? Of the manic-depressive
? Of the psychoneuroses ? Of conflicting hypo
ere are many as Dr Cameron points out There
theories of prenatal infantile and childhood
ing of environmental stress of the influence
cultures When it is pointed out that not all
who undergo the (alleged) hurtful experiences
mentally ill one falls back on constitutional
dition But what this really is, or how it can
tated we do not know It is obvious that a
ble amount of research will have to be under
fore we can talk with confidence concerning the
of mental illness and until we are able to do
annot organise prevention in a scientific manner

This brings me to the important point I wish to make. It is vitally urgent that large sums of money should be allocated for research in psychiatry The sum allotted at present is insignificant in relation to the complicated problems to be solved Very few of the hundred-odd mental hospitals in England are given funds for research as far as medical personnel is concerned they are under staffed and can barely cope with the programmes of therapy let alone research May I here quote the annual report of the Mental Health Research Fund

> Clinical research though not without growing points, lags far behind clinical research in general medicine Research pecifically directed to mental health whether in the clinical r the fundamental field is far smaller in volume than that directed to problems of general medicine and this reflects the fact that it still interests and attracts far fewer of the best brains

Until funds are forthcoming and until the fruits of research are gathered we must resign ourselves to half the hospital beds in the country being occupied by mental cases

Park Prewett Hospital
Basingstoke　I ATKIN
Physician Superintendent

## TREATMENT OF IMPETIGO

SIR,—The Ministry of Health [1] has pointed out that the general use of aureomycin and terramycin either systemically or locally in minor staphylococcal infections will foster the emergence and spread of resistant strains Stewart [2] and other investigators have emphasised the dangers of resistance or sensitisation through the topical use of important antibiotics which are administered systemically while Russell [3] has stated that the topical application of aureomycin or terramycin may induce infection due to gram negative organisms especially proteus

In the past four months I have treated about 30 cases of impetigo with 'Graneodin ointment each gramme of which contains 2 5 mg of neomycin and 0 25 mg of gramicidin

Neomycin is highly active against many gram positive and gram negative bacteria while gramicidin increases the activity of the product against streptococci and other gram positive organisms. Neither antibiotic is normally given systemically although neomycin may be given by mouth for intestinal infections because it is not absorbed to any appreciable extent When given parenterally neomycin has some nephrotoxic and ototoxic effects; gramicidin is too toxic for routine injection and is absorbed to only a very limited extent from the gastro-intestinal tract The topical use of this combination does not, therefore involve risks of resistance or sensitisation to antibiotics which are required for systemic administration and its activity embraces many gram negative organisms as well as gram positive bacteria.

No case of sensitisation to graneodin ointment was encountered in this trial Leslie and Harvey [4] also recorded no sensitisation in their investigation which embraced 105 cases of various skin infections The duration of therapy in my series however was short the majority of cases required four or five days treatment and only 2 cases were treated for as long as eight days No other agent was used

All the patients were children except for 3 young adults. The patient (or in the case of a child the parent) was instructed to rub the ointment well into the skin lesion three times daily and not to apply anything else In very young children, the lesions were covered with gauze and bandages.

Most of the cases were fairly early ones and rapid response was the rule the majority showing healing on the third or fourth day There were no relapses, but a few cases required a second short course of treatment where two or more members of a family had impetigo and reinfection occurred

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[1] See *Lancet* 1954 ii 520
[2] Stewart G T *Ibid* p 117[illegible]
[3] Russell B *Brit. med J* 1954 ii 1016
[4] Leslie G Harvey G *Brit J Derm* 1954 66 11[illegible]

Although I have tried most of the agents recommended for the treatment of impetigo, none has proved as effective as graneodin ointment

Walton, Liverpool J McMASTER

## PERFORATED PEPTIC ULCERS

SIR,—In your issue of Jan 22 Mr Moore gives an excellent account of his successful results in the treatment of acutely perforated peptic ulcers One wonders, however, whether he is justified on his own findings in reaching some of the conclusions he did For example, he attributes the satisfactory results in three very seriously ill patients with perforations to operation, despite the fact that it is likely that the energetic resuscitative measures employed played at least as much a part as the operation, and he uses this as an argument in favour of operative treatment for seriously ill cases It is possible that his three patients who died on the conservative management were also treated by energetic resuscitative measures, but there is no mention of this in his paper If they were not so treated then surely it is rather unfair to blame their deaths on conservative management

The conclusions he draws from his table IV are much too general for the type of data he has assembled there Each section of the table shows a very variable mortality In the first part this ranges from no deaths to a 20% mortality, in the second, it ranges from 1 8 to 17 5%, while in the third, it ranges from 0 to 17% The various series included under each of the three headings certainly do not appear to be identical, nor are their ages mentioned In view of this great variability, it would be unwise to conclude, as Mr Moore does, that whichever method of treatment is used the results are apparently much the same

Department of Surgery
Medical School,
Dundee JOHN GRIEVE

## METHYLPENTYNOL AND HABIT FORMATION

SIR,—Two recent articles in your columns have again dealt with methylpentynol,[1 2] and its use—not only as prescribed by a doctor but also "unofficially"—seems to have become more widespread It has frequently been described in the popular press as "not habit forming,"[3] and whilst our own earlier experiences with this drug did not show any evidence to the contrary,[4 5] this happy state of affairs has unfortunately not continued for long

Recent experience with psychopathic and neurotic alcoholics has, not unexpectedly, shown habit formation and addiction with the use of methylpentynol to be a definite possibility in the case of unstable personalities We now know of at least six alcoholics who took large quantities of this drug Two of these developed a confusional and highly emotional state, with slurring of speech and ataxic gait, after taking up to 20 capsules for two or three days, while others (not personally observed) seem to have taken equally large numbers for a somewhat longer period All these alcoholics had, as far as we know, also been in the habit of taking other hypnotic drugs to excess

In this connection it may perhaps be mentioned that a number of outpatients stated that methylpentynol seemed to increase considerably the effect of alcohol when taken together, an effect resembling the synergistic action of alcohol and barbiturates[6] The possible synergism between barbiturates and methylpentynol,[7–9] and the fact that a death after taking 18 to 24 capsules of the drug has been reported in America,[10] should also be kept in mind when considering the danger of unrestricted self medication by the public

Apart from these drawbacks, in ou methylpentynol has proved a satisfac normal amounts non toxic both on clinical investigations As far as alcoholics are co of whom appear to be unable "to hand drug in moderation,"[11] methylpentynol still appears to be preferable to the ot where a hypnotic is necessary. Its use, how be discontinued (and this can be done as soon as possible after the first few days

It is regrettable that members of the apparently still be able to purchase large this drug so easily without a prescription, advice of the Council of the P that it should be supplied only on a as this may possibly bring a valuable drug through excessive and indiscriminate use

Warlingham Park Hospital
Surrey M

## BARBITURATE POISONING

SIR,—The treatment of acute barbitur remains highly controversial, with the adv use of analeptics on the one hand,[13] and the servative approach on the other[14 15] II experience of both approaches I have becom to the latter

Dr Lurie,[16] who has found co this disorder, writes "The action of in suppressing pathological reactions unexplained, and we are certainly not in offer any explanation of its rôle in barbiturat

Einhauser[17] showed in rats that initially on the vasomotor centre causing collapse, and later acted directly on the vessels causing increased vascular perm collapse Experimentally Menkin[18] and found that vascular permeability is decre administration of corticotrophin In p thrombocytopenic purpura Faloon et al[20] temporary but consistent increase in capill during treatment with corticotrophin

Presumably this temporary reduction permeability by corticotrophin might acc striking results obtained by Dr Lurie in coma

Royal Infirmary,
Manchester IAN A.

## ISOBEL CRIPPS CENTRE

Mr Charles Neil writes

In answer to Dr Barlow I must point out the of suspecting," or "not suspecting" the prese not on me, since the *only* cases that are taken care are those who come to improve some skill violinist, the dancer, or the golfer I maintain every safeguard that can be taken, like the ph with whom we enjoy a friendly and coöperative,

When our methods and our institute have securely established, there will then be no need as is now so in the medical profession, but wa In the mean time, our present "intensive adv paign" consists of one advertisement a fort "lectures and specialised training" column of *Statesman*, and great care is taken to see that mislead, or claim too much Dr Barlow had 1950 to find one which contained a doubtful phr I had stopped as soon as my attention was dra

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1 Bourne G *Lancet* 1954 ii 522
2 Trotter P A *Ibid* p 1302
3 *Evening News* July 14 1954
4 *Brit med J* 1954 i, 760
5 *Lancet* 1954 ii 143
6 *Brit med J* 1953, i 1269
7 Gialdroni C Grassi C *Atti Soc Lombarda Sci med biol* 1952 7 90
8 Zoboli P *Boll Soc ital Biol sper* 1953, 29 111
9 *Lancet* 1954 ii 1332
10 Cares R M Newman, B Manceri, J C *Amer J clin Path* 1953 23, 129
11 Sedatives and the Alcoholic New York 19
12 *Pharm J* July 31 1954 p 80
13 Koppanyi T Fazekas, J F *Amer J med Sci*
14 Nilsson, E *Acta med scand* 1951 suppl 253.
15 Locket S Angus J *Lancet*, 1952, i, 580
16 Lurie, I *Ibid*, 1954, ii 601
17 Einhauser M *Klin Wschr* 1939, 18 423.
18 Menkin, V *Proc Soc exp Biol* N Y 1951 77
19 Benditt E P, Schiller, S, Wong, H, Dorfman
75, 782
20 Faloon W W, Greene R W Lozner, E L
1952 13 12

# Obituary

## EDWARD MELLANBY

, K.C.B. M.A., M D., Sc.D Camb D.Sc LL.D
F.R C.P F.R.S

e sixteen years 1933–49 Sir Edward Mellanby commanding position in British medicine as of the Medical Research Council This period of rapid development both in science and in the y of science and if, as we believe conditions al investigation in this country are still excep good no small credit should go to Mellanby for often right in his opinions and his actions In ys he was not well cast as an administrator for ot always appear either judicial or receptive and be careless of other people s feelings But his, he was a man of unusual vigour and unusual d himself an investigator who never ceased ting—and usually got results He took and held l post because he saw how it is that, in so far as work is organised at all e organised by those who nd it. But he also used influence to ensure so could that the knowledge y such work was applied public benefit. As the Research Council said o war the results of the population during the have been a triumph for o had been engaged in al research for the past ars and both as investi l Government adviser part lumph was Mellanby s

[Walter Stoneman

on of John Mellanby a ler in West Hartlepool one of four brilliant of whom one died young thers were A. L Mellanby of engineering at Glas l John Mellanby F.R.S of physiology at St s Hospital Edward was to and carried all before his school at Barnard but he deliberately gave s on going to Cambridge where he had won a ip at Emmanuel College At Cambridge he s a research student even before starting clinical St. Thomas s and he published a paper on nd creatinine in the *Journal of Physiology* before g in 1910 Thereafter he was demonstrator ology at St Thomas s, held a Beit fellowship 913 joined the staff of King's College for Women er on physiology His interests at this time the chemical study of cyclical vomiting and the sm of lactating women; and while at King s e recorded experimental work on diarrhoea and in children, and produced in 1919 for the Research Committee (as it then was) a major n experiments on the absorption of alcohol en for the board then controlling the liquor trade fruitful inquiries had begun, however when on the advice of Gowland Hopkins, the Medical Committee gave him a grant to study rickets. comprehensive experiments on puppies he was rovide in 1918 the first conclusive proof of the of an antirachitic vitamin—and also inci to warn *clinicians against* looking at accessory tors separately from other elements of the diet the general metabolism[1] Two M R C special on rickets followed the first in 1921 and the n 1925 By this time he was further exploring ency of cereals to inhibit the formation of bone arousing opposition by his comments on oatmeal r on in 1937 he showed that the rachitogenic o in cereals was phytic acid whose action had utralised by a sufficiency of calcium in the diet.

From his chair of physiology in London, Mellanby moved in 1920 to Sheffield where he became professor of pharmacology and physician to the Royal Infirmary Here he was clinician as well as teacher and investigator and it was his custom to lecture at 9 A.M. see his patients in the wards and then spend the rest of the day at the field laboratory which had been built for him. (The story is told that three months after the grant for this laboratory had been approved he was asked whether he would not soon be submitting plans To which he replied that he had already been at work in the new laboratory for three weeks.) In 1914 he had married May Tweedy, and at Sheffield there was good scope for those related yet independent investigations which made the scientific symbiosis of the Mellanbys so happy and so successful

In 1931 he was made a member of the Medical Research Council and two years later he was appointed secretary At this time the foundation of the council s activities had been laid and its position as an important factor in the scientific life of the country had been established by the work of the late Sir Walter Fletcher but the organisation nevertheless remained a small one That it would expand so greatly during Mellanby s period of office and under his guidance was hardly expected at the time of his appointment. He was then known as a devoted research worker of great scientific distinction in the field of nutrition and it was a matter for some surprise that he was willing to leave his laboratory for an administrative post.

In point of fact of course Mellanby never did allow himself to lose direct contact with laboratory work and this was characteristic In the early days of his secretaryship he kept experimental work going by weekend journeys to his old laboratory at Sheffield , after the building of the Nutrition Laboratory at Mill Hill most of his weekends were spent there—even during the war when the burdens and responsibilities of his official work were more than most men would care to carry as their entire occupation Nor was his laboratory work during this period by any means a nominal occupation his research on the effects of vitamin A on bone growth gave him the material for an impressive Croonian lecture to the Royal Society while his discovery in 1947 that the current treatment of flour with agene produces a substance toxic to dogs has already done much to draw attention to the whole question of treatment of foods with chemicals.

In Sir Charles Harington s words

> It was this single minded devotion to the cause of scientific research in medicine particularly research in the laboratory that determined the character of Mellanby s work as secretary of the Medical Research Council It made him always insistent on the principle that the interests of the research worker must come before those of the organisation He was shrewd in administrative affairs and he showed vision in guiding the council into new developments moreover his strength of character enabled him to assume heavy responsibilities without complaint On the other hand he never gave the impression of being happy in administrative work such work was a means to an end and was tolerable only in so far as it helped the advance of scientific work, and it could at times be the cause of impatience nor was it everyone who realised that this impatience was on occasion partly assumed with the deliberate intention of provoking a vigorous and uninhibited reaction and of so getting rapidly to the root of the matter
>
> “This is not to say that Mellanby did not enjoy as would any man of strong character with confidence in his own judgement the power that his position gave him to influence the development of medical research and its applications to many fields of human endeavour both in peace and in war he certainly did derive satisfaction from the growing impor

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[1] *Lancet* 1919 i, 40

tance of his job, but what gave him unalloyed joy was the manifestation of its success in new scientific discoveries to which he could feel that the council's work had contributed

"All this meant that whilst over administrative matters there might be barriers to be overcome with Mellanby, there was never any need for difficulty when the subject for discussion was a purely scientific one Indeed, any research worker who was sincerely trying to do a good job could be sure of Mellanby's patience, sympathy, and encouragement, and there are many in the service of the Medical Research Council and outside it who owe him much "

One of his juniors, C M F, writes

"Mellanby never tired of declaring his unfitness for the job of secretary of the M R C but he really knew that he was well fitted for it, as the pleased twinkle in his eyes declared if you asked him how it was that the whole show ran so well and contributed so much to medical science under his guidance The secret was that he had an unerring sense of the directions in which progress could be made and remarkable judgment of the men likely to succeed in each field of endeavour Having chosen his man he provided constant if critical support, but he never directed or constrained A discussion with him was always profitable, but often in unexpected ways He might not answer the problem which you brought to him, but would suggest a new approach to some neighbouring problem which had not till then seemed relevant And always there was the stimulus to *discover* He classified scientists as 'discoverers' and the rest He was remarkably outspoken, often almost alarmingly so, in his comments upon those whose work he considered valueless, but if events proved him wrong, he was always generous in admitting it

"He was at his best during weekends at the Nutrition Laboratories at Mill Hill It was incredible that he should be able to dismiss all his administrative burden each Friday evening and then settle down to his own research as if there had been no interruption Part of the secret no doubt lay in the companionship given to him by his wife whose scientific interests lay so close to his own The fire of the scientist's curiosity lit up his whole great frame as he took one round to see his animals and talked of his experimental plans or of the benefits he saw accruing to mankind from the application of his work

"There was no question of retirement after he left the secretaryship of the M.R C There were more discoveries to be made—'without any elaborate apparatus,' he would insist—and he went on making them to the very end His example and his memory will continue to inspire all those of us who knew him, respected him for all that he was and did, and, though he would scarcely have believed it, had a real affection for him "

In his Harveian oration to the Royal College of Physicians,[2] Mellanby sought first to show that though "the words control and bureaucracy have a disagreeable sound particularly in the ears of those searching after truth by experiment," State control of medical research can be compatible with freedom to the investigator He also set out the policy which the council was then unfolding and which has since developed so much further —including the grafting of its own research units on to various hospitals, universities, and other institutions, to the considerable benefit of both graft and stock In discussing such control he admitted that mistakes in appraisal are inevitable "relatively poor workers may stand, especially in the eyes of their near colleagues, on a pedestal of distinction and, much more serious, the first-class discoverer and his work may go unrecognised " But he felt that the constitution of the council was a substantial safeguard against error Elsewhere[3] he wrote 'The test of the acceptability of a discovery depends on whether it is true and not whether it seems sensible or even whether it can be verified by the statistician " Always he pressed the need for knowing more, pointing out that any State scheme affecting health—however large, however costly, however well administered—can be only as effective as medical knowledge at the time allows it to be[4]

After his retirement from the M.R.C he
India and to Australia, where his advice on t
of research was eagerly sought and warmly
In the international field he was well known
of the International Conferences for Stand
Vitamins (1931, 1934, and 1949) and of the
Technical Commission on Nutrition He w
many years chairman of the Colonial Medic
Committee

Mellanby's almost innumerable distinctions
Bisset Hawkins, Moxon, and Baly medals of
College of Physicians, to which he was elected
the Royal and Buchanan medals of the Royal
which he became a fellow in 1925 He was an
of the Royal College of Surgeons of Edinburgh
granted honorary degrees by the Universities
Cambridge, Sheffield, Birmingham, St Andrews
Belfast, Melbourne, Adelaide, Witwatersrand, O
Oslo He was Fullerian professor of physiology
Institution from 1935 to 1937, and was made
fellow of Emmanuel College in 1946 In 1937 he
K.C B, and in 1948 G B.E

Sir Edward Mellanby died last Sunday,
had been engaged in experiments an hour

## CHARLES HERBERT HAMPSHIRE

C M G, M B B Sc Lond, F R I C, F.P.S

As we announced last week Dr C. H.
secretary of the British Pharmacopœia Comm
1929 to 1950, died in London on Jan 25 at the

He was the youngest child of a large famil
and from the local grammar school was appre
pharmacist in his native town In 1905 he
School of Pharmacy of the Pharmaceutical S
a Jacob Bell scholarship, and later, as a qu
acist with most of the prize medals of his year
the staff and proceeded to a degree in chem
fellowship of the Institute of Chemistry
turned from a teaching career to take the position of chief pharmacist at University College Hospital, and, with his new responsibilities mastered and his department organised, he determined to qualify in medicine, not with the intention of practising but the better to fit himself for the expansion of his hospital duties

A new direction in his career came in 1929 The General Medical Council, in accordance with their obligations under the Medical Acts, had published the fifth edition of the *British Pharmacopœia* in 1914, and by the mid-1920s it was clear that
the organisation of the detailed work of rev
pharmacopœia required strengthening in ord
pace with the advances in materia medica
and pharmacy In 1928 a subcommittee of
mittee of Civil Research, appointed at the
the Lord President, recommended that the
of future editions should be undertaken by a
working under the general direction of the
the following year Hampshire was appointed
and his twenty-one years of office saw t
*Pharmacopœia* achieve an excellence which
throughout the world He brought wide kn
unstinted energy and devotion to the
work of the commission The new pharmaco
was followed by a substantial addendum in 19
war-time addenda preceded a larger and compl
pharmacopœia in 1948 He retired from the
of the commission in 1950

Early in his career he became interested in t
tion of national pharmacopœias, and he was
chairman of the Technical Committee of Ph

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[2] *Ibid* 1938 ii 929
[3] *Brit med J* 1949 i 921
[4] *Lancet* 1939, i, 1063

set up in 1037 by the League of Nations In
World Health Organisation re-established work
eparation of an *International Pharmacopœia*, and
re was again elected chairman of the expert com
nd presided over many sessions at Geneva and
in the United States In 1951 he was able t
he first volume of the *International Pharmaco*
the assembly of the Fédération Internationale
eutique in Rome. His enthusiasm for the work
unabated, and to the end of his life he was busy
reparation of further volumes.

through the years he turned from his main busi
pharmacopœias, the hobbies he pursued consti
nost a career in other branches of pharmacy and
For ten years he served as an honorary
of the British Pharmaceutical Conference and
airman from 1932 to 1934 He was editor of the
*Journal of Pharmacy and Pharmacology* from
tion in 1928 and continued in office when it
monthly publication in 1919 He had planned
next month on reaching his 70th birthday He
uthor of numerous papers, mainly on aspects of
utical chemistry For many years he was a
of the board of examiners of the Pharmaceutical
and of the Royal Institute of Chemistry and
ntly he was on the Board of Studies in Pharmacy
iversity of London. In 1919 he was appointed

was a certain Northern toughness in Hampshire s
amounting sometimes almost to an aggressive
ness, which he showed in the pursuit of the
had at heart. His skill and devotion to his chosen
ned the respect of medical men and pharmacists
countries, and he will be much missed not only
n but also in Geneva. The following tribute
m Prof J A Gunn:

appointed secretary to the commission in 1929
pshire soon proved to be ideally equipped and
for the varied kinds of work involved in the compila
harmacopœia. The current *B.P 1914* was hopelessly
te as was revealed by the large number of new
l preparations introduced into and the even larger
of useless or redundant drugs deleted from the
Hampshire tackled his side of the work with unflag
The work was congenial to him his previous dis
l career had given him a wide knowledge and
experience of pharmaceutical science and he also
eal qualifications: when under a reconstituted
n, the work of preparing a second pharmacopœia
n his previous experience was invaluable in facili
smooth running of the work of the commission and
ately remained in office until after the publication
ayed owing to the war of the *B P 1948*

associated with him continuously during the long
preparation of both pharmacopœias, more closely
e last ten years when I acted as chairman of the
n. The work was especially difficult during the
d when numerous addenda to the *B P 1932* had
lished to keep the pharmacopœia up to date and to
ubstitutes for important drugs no longer available
n stumbling blocks cropped up The General Medical
remises in Hallam Street were bombed and many
pœia records were destroyed The commission had
e to temporary and less convenient quarters. It was
ult sometimes to get the requisite paper and binding
h the addenda For some time when under the
s meetings of the full commission had to be limited
r urgent decisions were often left to the chairman and
with power to consult individual members of the
on as seemed necessary I then made frequent
to London for personal consultations with Hamp-
this way I got to know him intimately and acquired
ing admiration for his abilities as well as a lasting
for him as a man No differences of opinion (and
re bound to be some) ever left any ill feeling or
ed our friendship The strenuous, unremitting
netimes frustrating work of the war period
Hampshire s health and I think he never quite
l.

hose who have had pharmacopœial experience can
d the vast amount of meticulous work that goes to
ng of a pharmacopœia. The standard for a single
physical property of a drug may involve collection of data from manufacturers and from academic and private pharmaceutical laboratories, checking the statements in the commission s own laboratory and discussion of the data by an appropriate committee and finally by the full commission but all that appears in the final pharmacopœia may be Melting point, 164 5° to 166 5° It is the same with every detail in a monograph in a volume of over 800 pages

In all this work Hampshire was the catalyst He had in full measure the requisite patience learning and temperament Apart from his many other activities and achievements for his pharmacopœial work alone he richly deserves to be held by the medical profession in honoured memory

Dr Hampshire married in 1915, Miss Grace Mary Taylor She died a year ago and he is survived by his daughter

## FRANCIS HARPER TREHERNE

### K C M G., F R.C.S.E

Major General Sir Francis Treherne who died on Jan 30 at his home at Woodbridge, Suffolk at the age of 90, took part in the Egyptian war of 1882 and he ended his long and honourable record of active service as director of medical services to the Mesopotamian Field Force in the 1914–18 war

He studied medicine at St Bartholomew s Hospital qualifying in 1881 He began his service in Egypt in 1882 and took part in the campaigns of the Sudan and the Nile in 1884 The same year he took the F.R C.S.E. In 1893 he was posted to India as surgeon to the commander-in chief From 1899 to 1901 he again saw active service in the South African war and he was present at the battle of Lombard s Kop which led to the defence of Ladysmith. For his services he was mentioned in despatches. He was promoted lieut -colonel in 1902 Later he was posted once more to India and served on the North West Frontier in 1908 In 1911 he became A.D.M.S India and the following year he was appointed honorary surgeon to the Viceroy

At the beginning of the 1914–18 war he served at first with the British Expeditionary Force. With the rank of surgeon general he was in 1915 appointed D.M.S to the Third Army and received the honour of C.M G In 1916 he took up the appointment of D M.S to the Mesopotamian Force For his services at the actions of Kut, Diala and the capture of Bagdad he was twice mentioned in despatches and he was promoted K C.M.G In 1917 he returned to this country and served as D D M.S London district and as inspector of medical services before he retired in 1919 with the rank of major-general

By his first marriage to Meliora Farmar who died in 1891 he leaves two sons. In 1900 he married Norah daughter of General Sir Frank Turner and there was a daughter by this marriage

## JAMES HARDIE NEIL

### C.B.E. D.S.O F R.A C.S., F.A C.S

Mr J H Neil who died in Auckland on Jan 28 was a distinguished aural surgeon and a well known public figure in New Zealand

He was born in 1875 and studied medicine at Otago University His painstaking dissections of human and animal lungs and his early mastery of the technique of bronchoscopy established him as a pioneer in his chosen field of otolaryngology For many years he was aural surgeon to Auckland Hospital and to Mater Misericordiae Hospital, Auckland His textbook *Ear Nose and Throat Nursing* reached its fourth edition in 1918

D R writes: Both in peace and war Hardie Neil served his country in many capacities During the South African war he was surgeon captain to the 4th New Zealand Mounted Rifles and in the 1914–18 war he commanded No 1 New Zealand Rifle Brigade Field Ambulance In the second world war he was appointed deputy director of civil defence for the Auckland region He held office as president both of the Auckland division of the British Medical Association and of the Pan Pacific Surgical Association; and at the time of his death he was president of the New Zealand League for the Hard of Hearing which he had helped to found

"He will be affectionately remembered by his colleagues in many walks of life—medical, civic, and military"

Mr Hardie Neil married Miss Mary Elizabeth Coates, she survives him, with four daughters, and a son who practises his father's specialty

## JAMES WHILLIS

M D, M S Durh, F R C S

As one of the editors of *Gray's Anatomy* Professor Whillis was accorded respect by medical students all over the English-speaking world By the smaller, but ever growing, number of his own students at Guy's Hospital he was also accorded affection and trust

He was born at Newcastle upon Tyne in 1900, and was educated at Carlisle Grammar School In 1922 he graduated M.B with first-class honours at the University of Durham The same year he was appointed demonstrator of anatomy in the university, and later he became lecturer While holding this appointment he proceeded to the higher degrees of M.S in 1925 and M D in 1930 Two years later he took the F.R C S

In 1935 he came to London to take up the readership in anatomy at Guy's Hospital His chief, Prof T B Johnston, soon drew him into the constant and exacting work of preparing successive editions of *Gray*, and for the last four editions Whillis acted as a co-editor The first edition of his own textbook, *Elementary Anatomy and Physiology*, appeared in 1938 In it he effectively introduced the student, while still at the outset of his studies, to the real significance of the anatomical facts and to the interdependence of structure and function At the outbreak of war in 1939, together with his colleagues on the staff of Guy's, he extemporised what was in fact a residential university institution from an empty nursing-home and four large private houses at Tunbridge Wells The success of this transformation was equalled only by the speed with which the work of adaption was planned and carried through The standard maintained under continually changing and increasing difficulties made it clear that all concerned were exceptionally competent and reliable, and Whillis's appointment to the chair of anatomy in 1948 was the logical recognition of his share in this work, and of his organising and administrative capacity and teaching ability

For some time Whillis had taken a lively and constructive interest in the activities of the Chartered Society of Physiotherapy, and in 1950 he was elected chairman of the council During his term of office the World Confederation for Physical Therapy was inaugurated, and he took the chair at its first congress which was held in London in 1953 Of this side of his work W S C C writes "Since the late war the society had grown enormously both in the public and professional estimation, and had begun to wish for more specific recognition in the academic field As chairman Whillis brought to this project an almost boyish enthusiasm, and his personal influence can be seen especially in the revised examination syllabuses of the society His chairmanship provided him with one of his major interests, and his enforced retirement last year, as the result of his illness, was a great grief to him His cheerful dynamic presence will be much missed, not only in the chartered society but among all those concerned with the future activity and status of the ancillary medical professions"

T B J writes "Whillis was especially interested in the anatomy of the living subject and he had done much work, not all of which has been published, in an [illegible] the movements concerned with swallowing [illegible] speech production He was anxious to retain his clinical interests, and he was a frequent visitor to Stoke Mandeville Hospital, Grinstead Latterly he had been much preo the study of proprioception and the possibilit for practical application, and he had succeeded that a prosthesis can be operated by the currents produced by contracting muscles. tus was demonstrated for him by his summer meeting of the British Orthopædic in 1954 As a teacher he was intensely prac approach, always stressing the functional subject, and, as one result, he had no difficulty ing the interest and attention of his students also deeply and permanently impressed by draftsmanship with which he illustrated his time to time He was a great worker and a m interests He had, for instance, a surpr knowledge of antique furniture, and for some had acted as the director of the pho illustration department at Guy's. In his own there was always a noticeable atmosphere of and informality, and these good internal extended to all the other departments. His death at the age of 54, on Jan. 27, has rob anatomy of one of its most active minds and as a serious blow to Guy's"

In 1926 he married Miss Dorothy Margaret survives him with one son

A memorial service for Dr H K. Waller will be chapel of the British Hospital for Mothers and Bab Street, Woolwich, S E 18, on Thursday, Feb. 17,

## Appointments

**BOLZ** I A, M.D Vienna D P H joint M.O., to County Council and deputy M.O H for Hampstead

**BREWER** D J M B Lond asst chest physician, Hartlepools tuberculosis administrative area.

**CANNON**, P G, M B St And D P H asst county M Beccles, the Bungay Halesworth, and Leiston and the Blyth and Wainford rural districts

**DEANS** HILDA A., M B Aberd, D P H asst M.O.H. preventive services), Dundee

**LEHANE**, NORA M A, M B N U I T D D asst school

**MACGREGOR**, G A M D Glasg, D P H asst area No 6 (Crook), and M O H for urban distr and Willington, Towlaw and rural district of Durham

**MACKENZIE** A C M D Edin D P H M O H Shrew

**MARTIN** C C D, M CH Belf F R C.S I senior Bury and Rossendale Hospitals, Manchester R.H

**MILES** T F M.R C S F F A R C.S D.A. consultant Cardiff area and Caerphilly district.

**RICHARDS** N A, M D Adelaide, M.R C.O G part-time obstetrician and gynæcologist, Stafford group R.H B

**SIMMONS** G H A, F R C.S consultant surg Hospital, Manchester

**THORN**, P A, M D Lond., M R C P D C.H part-time physician mid Worcestershire group Birmingham

**TREASURE** E R. M.B Wales, F R C.S.E. asst. (S H M O), Morriston Hospital, near Swansea.

**WILLIAMS** K M., M B Birm, D P H D I H principal Westminster City Council and Holborn borough

**Colonial Service**

**CLARKE** G J, M R C.S D T M &H S.M.O St Hele

**GRIFFIN**, P N M B Sheff M O Dominica, W

**HALL CRAGGS**, E C B M B Camb M O Uganda

**MOORE** S R. W, M B Belf M.O, Sierra Leone

**MURPHY** C W E M B Dubl, D.P.H special (anæsthetist) Aden

**PURSER** MARGARET J, M.B M O, South Pacific H Fiji

**RAJCOOMAR**, TERMAN, M B Patna, D T.M.&H M.O.

**SCHOYERER**, R A F, M D M O, Gold Coast

## Births, Marriages, and Deaths

### BIRTHS

**HALNAN**.—On Jan 30, at University College Hospital, (née Booth) wife of Dr Keith Halnan—a dau Mary)

### DEATHS

**MALCOMSON**.—On Jan 24 Greer Edmund Malcomson M.R C P D P H colonel I M.S retd of 23, John s Wood, London, N W 8, age 76

# Notes and News

## ALESCENT HOME FOR SERVANTS OF THE CROWN

King Edward VII gave Osborne House to the nat on
ne of his coronation it was decided to use it as a
ent home for officers from the Royal Navy and th
nce it was opened 50 years ago its scope has extended
w serves a large group of the servants of the Crown
e following men and women are eligible for admission

a) Serving and retired regular officers of the Royal Nav
y and Royal Air Force and officers of the Commonwealth
es serving in the United Kingdom.

ing officers of the R.N.V.R. Territorial Army and
F V R.

fficers—that is, officers who have ever held a tempora
mission in the Forces

tablished and permanent unestablished members of the
Service

ing members of the Foreign Office and the Colonia
ice

—Serving regular officers of the Forces and membe of
Civil Service and Foreign Service

is made to serving officers and those recommended
inistry of Pensions. For others the charge is 10s a

the nursing staff there is a remedial gymnast an
nal therapist and a physiotherapist Emphasis is
habilitation and there is a hot pool for the treatment
atic diseases, fractures and poliomyelitis Strict
are not suitable and no cases of incurable illness
iness, or tuberculosis are accepted Patients are
in the early stage of convalescence but must be
dressing and looking after themselves On the other
ple surgical dressings can be carried out and dietetic
arranged. The average stay is for three weeks. A
ndon consultants visit Osborne each month to advise
governor who is also the medical superintendent
rs serving with the Forces contact is maintained
Naval, Military and Air Force hospitals and
ls of the three Services visit regularly

grounds there is a hostel where wives and relatives
commodated while officers are in residence and there
private golf-course a bathing beach and facilities
croquet, sailing and boating

ts for admission should be made to the house
and medical superintendent Osborne House East
le of Wight

## DICAL JOURNAL FOR CENTRAL AFRICA

L readers striving to keep their heads above water
elling torrent of medical journals must often pray
ise But, for all that the foundation of a new
sometimes clearly justified—for instance to form a
en groups with specialised interests, where no other
link exists, or to secure publication of work that
recorded but which otherwise might not be Both
d reasons underlie the initiation of the *Central
ournal of Medicine*[1] which has made a brave start
An editorial in the January issue remarks on the
cord facts of local interest, both for the information
in the area and for the benefit of those who come
our successors will be interested to learn of our
of practice what the prevalent diseases were and
oped with our problems and overcame our diffi
Moreover a busy doctor who sees an interesting
not find it easy to prepare a well referenced article
orking far away from a medical library and there
a journal that will consider publishing his collected
gain, there is scope for investigation of and reports
ent by witch-doctors. Not only will such a
e an anthropological value but it may provide a
od of treatment The journal's editorial board is
Dr Michael Gelfand Profits are to be devoted
ng a library in the proposed medical faculty of the
University; and the journal board has provided
stitution for handing over to an approved medical
thin the Federation of Rhodesia and Nyasa

## University of Oxford

On Jan. 20 the degree of B.M was conferred on the following

W G Cowell Audrey Grumitt G D H Lynne-Davies C S K Luck David Severs

In absentia

## University of Cambridge

On Jan. 22 the following degrees were conferred:

*M B B Chir* — R. A Carpenter P A Eckstein, J D Ellis I H C Hunt J B Pond, C J F Potter J T N Williams.

*M.B* —J W Blaxill L H Blonstein, J N Bodger D H Cameron, T D Carter L McL. Flowers, J N Godlee, Claudia M B Grigson L H Hurrell P J D Kirk, A H. Labrum, G J M. Milton Thompson C B Mortimer J N Rea C F Ridley Rudolph Schram, G C. Speckman

By proxy

## Royal College of Physicians of London

At a comitia of the college held on Jan 27 with Sir Russell Brain the president in the chair Dr G E. S Ward was reappointed external examiner in medicine for the Faculty of Radiologists

The following having satisfied the censors board were elected to the membership

J C Barker M.B. Camb, A W Beard M.B. Camb B.M Oxfd, W C Beeke, M.B Melb, H G T Bridge B.M Oxfd Stephanie J Carter M.B. Lond., H D Chalke L.R.C.P Anthony Coady M.B. Manc. A T Cook M.B Lond., captain R.A.M.C., Leon Cudkowicz M.D Lond D W Davies M.B. Lond., Pamela A Davies M.B Glasg., Felicity C Edwards, B.M Oxfd M. R. F Evans M.D Lond. H A Fleming M.D N.Z., E. G Gales, M.B Queensland Mary A Le C. Hills M.B Sheff W A Hudson M.B. Sheff R. B Hunter M.B. Edin H K. Ibbertson M.B. N.Z. K V Jones M.B. L'pool, captain R.A.M.C. W I N Kessel M.B. Camb J W Lance M.B. Sydney I H Lawrence M.B. Edin. D W Levy, M.B Cape Town Elizabeth A Martin M.B Lond. Stephen Mattingly M.B. Lond W K. Newton M.B. Lond D W Piper M.B Sydney J C Pond, M.B. Lond E. J Ross, M.B. Lond., G F M Russell M.B Edin Merton Sandler M.B Manc., E. P J Silberstein, M.B. Melb K S Somers M.B. Witwatersrand, C. F Stroud M.B. Wales G S Wakefield M.B. Lond. R. T Turner Warwick B.M Oxfd W C. Watson M.B. Glasg., Rose A J Whitelaw M.B. Birm. W H Wolfenden M.B. Sydney Joan F Zilva M.B. Lond.

Licences to practise were conferred upon the following who have passed the final examination of the Conjoint Board:

J R. Akers, N M Bailey G C W Baker Margaret A Barrie G D Blackledge, J P Booth P S Boulter H J Bradley A T Brown Elizabeth A Burns Enid J Cartwright Joan F Chaffers Evelyn B Clayton V E. Crapnell Hilary J Crawford D R Crockatt, Sheila R. Crosland I I Daimon D J Davies J G Davies Ann Davi , G H Daw, J A Dew Jones G S Dormand J W S Fyears W J Fessel Phyllis M Flenty J J Fryatt R H S Gibbs R C Giles J N Godlee, S A Greenhalgh R L Hargrove, Sheila C Hay W T Henry, I Janota Iona Johns P H Johnson Amar Nath Kalra R. W Kirkpatrick J K M M Kay Dorothy M Mahabir Eric Mallett A G Matheson Margrose E Meare I H Merry D M G Murphy G A Naylor M J O Neill, J E Pearson Jane Platnauer D I H Prosser Margaret A. Riddell Muriel I Riegelhaupt K P Robinson C R. Salmon L N Sargant Ali Ahmed Shaikh D J Sill G C Spackman J D Spink Frank Summers G G Temple L R Thomas I E Thoma , D J Thornton Allan M Thurrar M D A Vickers A W Ware Gladys M. L. West J P M William

The following diplomas, and those mentioned in our issue of Jan 22 (p 211) were conferred jointly with the Royal College of Surgeons

*D M R.D* —Habib Abdalla J M. Allcock J S Boyd Wilson, Purnendu Sekhar Brahma Russell Brain t'r J McC Carmichael P H Coldwell, R. V Dan, Mohanlal Gopalji Desai, J D De Villiers W W Frank Isaac Friedman F S Grebbel Isabella Grey Thomas K H Harper Neville Kaplan Chadalavada Krishna Rao E. W Moore, Mary G Murphy M N Phillips Sunil Kumar Baridhan Roy Basil Rosenberg Bankim Behari Roy Helen Sender J G Sowerbutts J H Stewart J V Todes

*D M R.T* —C F Baxter Sarna Bisey lhar K N H Low Helen M Mellor

*D Path.*—S S Epstein Monojmohan Roy Alexander Ewan J W Weston

*D.I M* —Vrajlal Narottdas Baxalla B C Blewold, Meatjie V Buhrmann H W C uran L D J Coore David Desi Raymond Doherty Thomas Galla, R. A Gelfer Samson Goldin Basil Gordon Mudiyanselage Gunapala Jayasundera, A F Johnstone M H B Joyce W A ker R D Laing R I Michael P McK Middlet r Marjorie A Morgan J G Neville Joseph Pisani Prahlad Kumar Ray G H Renton E. A Ritchie D H Rapsichitz A J E. Howe Ralph Sander C J Seager Ratnakar Vaikunth Shirvalkar R J Stott J L. Swift Leonard Tarlo J F Thomson, Eva Walker J P Whiteley W E. J Wilson E. A M Wood, P L. Walker

*D.P H* —Noshir Kaikhusrd Bharucha, Nuleer Cassell Joan M. St V Dawkins R. C Greenberg Mumtaz Husain D M O Lowry H R. Miller J I J O Keef Hla Kyaw Pe G W Piper G H G Poole J D Russell W J Wiebell

*D I.H* —A J F sex-Cater W N Taylor

*D T M.& H* —Abu Mohammad Mostaqul Haq G L. Little

On Thursday and Tuesday March 17 and 22 at P.M at the college Pall Mall East S W 1 Prof W Melville Arnott will deliver the Oliver-Sharpey lectures on Order and Disorder in Pulmonary Function.

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[1] d bi monthly £ per annum post free All nications should be sent to the Editor P O Box 2073 ary Southern Rhodesia.

## University of Edinburgh

Dr Alexander Kennedy, professor of psychological medicine in the University of Durham, has been appointed to the chair of psychiatry in succession to Sir David Henderson

Dr Kennedy, who is 46 years of age received his medical education at St Thomas's Hospital where he qualified in 1932 After holding house appointments there he took his M D and the M R C P in 1934 and specialised initially in pædiatrics He continued his postgraduate studies at the Johns Hopkins University and in 1936 was awarded a Rockefeller travelling fellowship in neuropsychiatry On his return to this country he became medical officer in charge of the children's department at the Maudsley Hospital while the present children's hospital was being built with the assistance of the Rockefeller Foundation In 1938 he was awarded the gold medal of the Royal Medico Psychological Association During the late war he carried out research in the psychology of parachute and commando training and took part in operations in the Western Desert Crete Greece and Yugoslavia Later, with the rank of lieut -colonel he was appointed head of a department dealing with the psychological aspects of military intelligence and subversive operations and was later an adviser on scientific intelligence in Germany After the war he returned to the Maudsley Hospital as senior physician and joined the staff of the Maida Vale Hospital for Nervous Diseases In 1947 he was appointed to the chair of psychological medicine at Durham He is also physician to the Royal Victoria Infirmary Newcastle upon Tyne and clinical director at psychiatric units in the regional mental health service In 1949 he was elected F R C P His publications include papers on hysteria, juvenile delinquency, experimental catatonia and organic psychiatry He has written radio plays under the pseudonym of Kenneth Alexander He has for many years been honorary medical officer to the Amateur Boxing Association and president of the medical commission of the Association Internationale de Boxe Amateur which has been responsible for radical changes in the rules governing international tournaments in the interests of the safety of boxers He has been a member of the medical executive of the Olympic Games and a past president of the British Medical Students Association

## Royal College of Obstetricians and Gynæcologists

At a meeting of the council held on Jan 29 with Sir Arthur Gemmell, the president, in the chair, Prof B P Watson was appointed William Meredith Fletcher Shaw memorial lecturer for 1955

The following were elected to the membership

R H O Bannerman David Barron H R C Benny D B Brown T I Cope A C Coulthard K D Drayton W A W Dutton B A Gavourin H S Gavourin, Tara Sankar Ghosh A P B Harston Beryl O Howie Beryl M Joles Mukulika Konar Wendy E Lewington J D Llywelyn Jones, Philippa M Ludlam C F Macdonald, J G Mathie Appuahandy Ariyaman Mahanama Mendis David Methuen Catherine H Mitchell Nanda Gopal Mukherjee Rathindra Nath Nag Chiew Seng Oon, Shephalika Prodhan, R T Sears Harendra Bahadur Sinha, D H K Soltau O S Treisman Yin Kai Tsao J K Tully, J A M Van Belkum

The following have been awarded the diploma in obstetrics

L C Steindel, D C Wilkins

# Diary of the Week

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FEB 6 TO 12

### Tuesday, 8th

Royal College of Physicians of London Pall Mall East S W 1

5 P M. Dr I A. Smiley Personal Factors in Accident Proneness (First Milroy lecture )

Royal College of Surgeons of England, Lincoln's Inn Fields, W C 2

3 45 P.M Dr E F Scowen Significance of the Endocrines in Breast Cancer (Imperial Cancer Research Fund lecture )

British Postgraduate Medical Federation

5 30 P.M (London School of Hygiene and Tropical Medicine Keppel Street W C 1 ) Prof J R. Squire Correlation between Laboratory and Clinical Findings in Hypersensitivity

Royal Society of Medicine 1 Wimpole Street W 1

5 30 P.M *Experimental Medicine and Therapeutics* Dr Sheila Sherlock Mr A G Riddell Dr W H J Summerskill Dr W T Cooke Hepatic Coma

8 P.M *Psychiatry History of Medicine* Prof Aubrey Lewis, Dr A D Leigh, Dr James Harper British Psychiatrists in the First Half of the Nineteenth Century

St Mary's Hospital Medical School Paddington W 2

5 P.M Dr H A Davidson Infertility in the Male

Chelsea Clinical Society

8 30 P.M (Rembrandt Hotel Thurloe Place S W 7 ) Lord Justice Denning Dr Robert Forbes Increase in Medical Litigation

Manchester Medical Society

8 P.M (Medical School ) *Surgery* Mr D S Poole Wilson Treatment of Hydronephrosis

### Wednesday, 9th

Royal Society of Medicine

4.30 P M *Physical Medicine* Dr T Anwyl Davies Dr J F Buchan Articular and Non-articular Rheumatic Complications of Venereal Disease

Institute of Dermatology, St John's Hospital Lisle Street W C 2

5 30 P M Dr Henry Haber Allergic Vasculitis

Manchester Medical Society

4.30 M *Pathology* Prof A C P Campbell Pathology of [illegible] plrosis (Presidential address )

## Faculty of Radiologists

At a recent examination for the fellowship th were successful

R G Britt, S Davis J G Duncan R G Grainger, J J W Laws H F March L L Ralph W diagnosis) E W Emery, H G Frank, R W Kunkler K A Newton, T M Prosser (radiotherapy).

## Colour Television in Pathology

The value of colour television in long-distance between pathologists was investigated at a symp last month in Washington, D C , by the Armed For of Pathology In one of the demonstrations at an operation in Philadelphia was televised to in Baltimore and Washington, who assisted in the

## Committee on Hospital Supplies

The Central Health Services Council have committee on hospital supplies with the follow reference

"To investigate and report on the organisation of hospital supplies including their purchase throughout the National Health Service"

The secretary of the committee is Mr L B Jacque of Health, Savile Row, London, W 1

## University College of the West Indies

On Jan 20, as part of its third Inter American the American College of Surgeons led by its A Blalock and the director, Major General Haw the university college and held two scientific were attended by seventy fellows of the college read by surgeons from the university college and ment medical service, and a tour of the univers hospital included demonstrations in the surgical departments

## Epsom College Centenary

On the occasion of the centenary the Queen and the Duke of Edinburgh are to visit the college The Queen has already sent a donation in appeal for £150,000 for improvements to college So far £12,000 has been contributed, including £1000 from Lord Webb-Johnson, £650 from the Medical Committee, £500 from the Medical In 100 guineas from the Notts Medical Committee from the Clerical, Medical & General Assurance the Norwich Union Assurance Society, and 50 the Berks Medical Committee Donations should the appeal secretary, Epsom College, Epsom, Surrey

Royal Faculty of Physicians and Surgeons of 242 St Vincent Street Glasgow

5 P M Prof A A Miles Serum Proteins in the Phenomena of Inflammation (Finlayson lec

### Thursday, 10th

Royal College of Physicians of London

5 P M Dr Smiley Personal Factors in Accid (Second of two Milroy lectures )

Royal College of Surgeons of England

5 P M. Mr P H Newman Spondylolisthesis lecture )

British Postgraduate Medical Federation

5 30 P M. Prof C H Gray Chemistry of the Porp

Institute of Dermatology

5 30 P M Dr J O Oliver Animal Parasites of the

Alfred Adler Medical Society

8 P M. (11 Chandos Street W 1 ) Dr James of Unity in Psychosomatic Medicine

Liverpool Medical Institution 114 Mount Pleasant

8 P M Dr P H Whitaker, Dr A J Robertson Pneumoconiosis Dr E Sherwood Jones Investigations of Disease as illustrated by on Blood

University of St Andrews Medical School, Dundee

5 P M Prof W I C Morris Sudden Death in Childbirth

### Friday, 11th

Postgraduate Medical School of London

2 P.M Mr J R Armstrong Differential Diag Pain

4 P M. Dr J W Todd Healthy Living

Institute of Dermatology

5 30 P M Dr P F Borrie Vascular Disorders

Institute of Laryngology and Otology, 330-332 Road W C 1

3 30 P M Mr Chapple Gill-Carey Epistaxis

Royal Faculty of Physicians and Surgeons of G

5 P M Dr E G Oastler *Cushing's Syndrome and* genital Syndrome

### Saturday, 12th

South East Metropolitan Regional Tuberculo

10 30 A M (London School of Hygiene and Trop Dr William Hartston Dr J F Galloway Measures in Pulmonary Tuberculosis

# B C G VACCINATION*

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vaccination has been a source of controversy e it was introduced by Calmette in 1922 Most who have studied the subject believe that such on confers considerable protection against sis; but the extent of this protection cannot ely assessed owing to our ignorance of allergy unity in tuberculosis, and the great difficulty g the importance of any one of the many social cal factors in this disease

accine is reasonably inexpensive and it is ult to prepare Except in two cases recently in Scandinavia (Thrap Meyer 1954) it has not wn to cause progressive tuberculosis in man and reactions are usually slight The technique of e vaccine is simple but requires care The dications are few There is strong evidence that ses resistance against tuberculous infection statistical proof is difficult to obtain These dged advantages of the vaccine are sufficient its use

## Manufacture and Cost of Vaccine

accine is not manufactured officially in this because we obtain from Denmark a satisfactory quite regularly and at low cost. The vaccine prepared in an entirely separate laboratory ist not be used for any other purpose The ld not be doing other bacteriological work that d to contamination of the vaccine with virulent All staff working in the laboratory must have ly *medical examination including radiography* st and a laryngeal swab or gastric lavage no ould be allowed to work in the laboratory even or porter without undergoing such an exami These precautions are necessary to prevent übeck disaster

blish such a laboratory requires considerable re and organisation While a very good and ply can be obtained regularly from Denmark there does not seem to be much point in e Treasury to allocate a considerable sum of r this purpose Manufacture of the vaccine ally has never been favoured by W H O or governments of countries where the vaccine een used But there can be no serious objection making freeze-dried vaccine, since this product, its comparatively long life, can be subjected ical and bacteriological examination before ed

g for wastage, the cost of the vaccine itself at orks out at about 3½*d* per injection for the cine and at about 2*d*. for the freeze-dried The average cost of vaccinating members of depends on the number tuberculin tested and er found to require vaccination In the Inter Tuberculosis Campaign (1952) during which lions were vaccinated it cost 7*d* to tuberculin 1s 1*d* to vaccinate each person while at s Hospital Dublin (1953) the figure in 1952 or tuberculin testing and 7s for vaccination. t been possible up to the present to give a this country

## Standardisation of Vaccine

s a living vaccine, whose potency depends on of the bacillus and the number of viable units contained in the inoculum The accuracy of the viable count is of great importance Methods have improved and the quantitative error in the Danish vaccine over a series of batches is now probably no more than 30% To this must be added the possible variation in the volume of vaccine injected intradermally and also the possibility of clumping

It is not improbable that in individual vaccinations the number of bacilli injected may vary by as much as 100% and it is therefore difficult to make comparable observations The variation in the bacillary content of the ampoules, which in the past has been as much as a hundredfold, is one cause of the spasmodic appearance of severe local reactions Furthermore the allergy producing power of the organism is related to the strain the medium on which it is cultured the age of the culture and also the grinding to which the culture is subjected. These are intricate bacteriological processes and unless they are made more uniform there will continue to be considerable variation between the vaccines issued by different laboratories

It has become evident that vaccines produced in Europe differ from those produced in South America For instance oral vaccination with the Dutch vaccine produced adenitis much more commonly than with the vaccine from Brazil. The vaccine from Mexico is distinctly less potent than that from Denmark.

In Dublin where Danish vaccine is used Dunlevy (1954) has found that the rate of relapse to tuberculin anergy at the end of one year is 1 8% In other parts of Ireland, where Swedish vaccine is used the rate is 20 72% This great difference may be partly due to differences in technique or in inherent resistance of the populations The dose of the Swedish vaccine is only two-thirds that of the Danish and this will influence the relapse rate as it is doubtful if there is a corresponding difference in the potency of the two vaccines

There appears to be no great variation between freeze-dried preparations This may be due to their stability after lyophilisation The Japanese strain (Research Committee of Tuberculosis Japan 1954) appears to have a slightly better power of producing tuberculin allergy than the French vaccine, possibly because younger cultures are used.

## Life of Vaccine

The life of the fresh vaccine is short Birkhaug and Darricarriere (1953) have shown that the bacilli begin to die after ten days. Whether this is important depends on the immunity conferred by injection of dead bacilli According to Palmer (1952) the presence of dead bacilli enhances the development of tuberculin-sensitivity but that does not necessarily mean that the conferred immunity is greater

Although the tuberculin-sensitivity after injection of mixed suspensions of live and dead B C G may be greater than that after injection of live bacilli alone there is little evidence that the duration of sensitivity is greater, or that the antibody response is as good Until further work has been done it is necessary to ensure a minimum amount of living bacilli in each inoculum which according to Sayé (1953) should not be less than one million organisms.

I agree with Birkhaug that the liquid vaccine should be used as fresh as possible and all the memoranda of the Ministry of Health have emphasised the need for this quite forcibly Certainly the vaccine should not be used later than fourteen days from the date of preparation Edwards and Tolderlund (1952) have shown that the vaccine is particularly susceptible to light and also to some extent to heat so the cold transport and storage in cool dark places is important

Although the freeze-dried vaccine as prepared in the past, is a poorer antigen than the fresh vaccine,

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i lecture, delivered at the Radcliffe Infirmary d, on Nov 10 1954 more stable and may be used up to six months from the date of preparation It is also less susceptible to light This instability of the vaccine to light and heat requires careful attention to technique, particularly in tropical countries

### Evidence of Protection

The object of B C G vaccination is to raise the body's resistance to tuberculous infection, particularly to primary infection by virulent bacilli There have been many controlled trials , but so far none is above statistical criticism, and we shall have to wait another two or more years for the results of the trials organised by the Medical Research Council

Observations in different countries indicate that non-vaccinated tuberculin-negative subjects are more likely to develop active tuberculosis than comparable vaccinated people, in the ratio of about 6 to 1 This figure has been arrived at by studying the results of ten surveys in different parts of the world in the years 1940 and 1953 (see Irvine 1954) Statisticians will frown on such haphazard calculations, but I think the figures indicate quite definitely that B C G vaccination does offer considerable protection against the development of primary tuberculosis Vaccination exerts little control over the development of postprimary lesions, although in some surveys the incidence and severity of these is apparently less in the vaccinated than in the unvaccinated So many factors influence the development of postprimary tuberculosis that I doubt whether it will ever be possible to study comparable groups for a long enough period to obtain accurate information on the remote effects of vaccination.

Active tuberculosis may develop in the vaccinated if the infecting dose of tubercle bacilli is large enough to overcome the resistance conferred by the vaccination

Recently, considerable evidence has been brought forward to show that B C G may have some influence in protecting against leprosy This is based on the fact that the vaccine will produce a positive lepromin reaction as well as a positive tuberculin reaction The difficulty lies in interpreting the lepromin reaction, which is by no means a simple manifestation of bacterial allergy Little definite can at present be stated, except that tuberculin and lepromin allergy are related

### Programme

At the beginning of the B C G scheme in this country, one of the great drawbacks to the use of the vaccine was the elaborate precautions that were considered necessary (Ministry of Health 1950) We have learnt by experience that these precautions can be relaxed a good deal without great risk For school-leavers, some local health authorities are attempting to reduce the procedure to the minimum for this country

They advocate one pre vaccination tuberculin test of 10 T U intradermally or by multiple puncture , then injection of B C G to the negative reactors, and no post vaccination tuberculin test, but only an inspection of the local lesion six weeks after vaccination Other local authorities have decided to test a sample of those vaccinated.

The argument used for this policy is that the conversion-rate is so high that it is not worth doing the post vaccination test to discover one or two per cent non-converters This is reasonable if there is substantial evidence of a satisfactory rate of permanent conversion in the area in other words, in each area the conversion and reversion rates should be determined before the post vaccination test is abandoned

Hertzberg (1947, 1948, 1949) has shown that the diameter of the local lesion in non converters was 0–2 5 mm and that of those in whom the local lesion was 4 mm or less only 56 4% were converted to tuberculin-sensitivity Where the local lesion was 5 mm or over, the conversion-rate was over 95% McKinstry and Darling (1953) had a [illegible] experience in Jersey If it is necessary to eliminate, as far as possible, the post
it would seem desirable to measure the
six weeks after vaccination, and to test all
it was less than 4 mm in diameter This
better than the random sampling at present
in some areas

In the Island of Timor, Oppers (1952) has
with the pre vaccination test and claims
plications have arisen There is general
accept this practice, but the objections to
been fully investigated It is claimed that the
of previously infected persons might activate
active lesion, or even reactivate a dormant
is also claimed that vaccination of tubercul
persons will cause serious local lesions that
time to heal, and it is reasonable to
allergic persons the fixation and multiplica
B C G in the skin at the site of injection
lupoid lesions to develop

Sayé (1953) in Barcelona has tested patie
active tuberculosis with 0 1 mg doses of
dermally , no lupus or lupoid lesions have oc
the local Koch's phenomena have been mild
not ulcerated or caused any troublesome sym

Foley and Parrot (1954), who have
problem for the past twenty years, persistently
that no untoward results follow vaccination
tuberculin testing , yet they recommend
vaccination tuberculin testing should be done
possible

The problem resolves itself into estimating
that might arise from giving B C G to persons
active or healed tuberculous lesions No harm
reported after intradermal B C G injections
in persons known to have active tuberculosis
there been many constitutional disturbances
oral vaccinations with freeze dried French
B C G Where B C G is used for treatment,
of patients show no reaction, but every now
clinical symptoms occur

Bøe, cited by Ustvedt (1950) also noted
disturbances in tuberculous animals that
B C G injections

Some light has been thrown on the process
infection by the treatment of active lesions
Gernez-Rieux et al (1947) found that, in the
cases, no general reaction occurred , but occas
B C G injection was followed by pyrexia,
rashes, and pleural effusion The symptoms were
those after injections of tuberculin, so pro
reaction to injection of B C G depends on the
of the tissues In the hyposensitive person no
tional disturbance will take place, but in the
sensitive there will be a constitutional respo
injection May it not be that the future co
superinfection with virulent tubercle bacilli
foretold by the response of the tissues to a viru
The possibility of using B C G to assess
infection has still to be explored

Much depends on the dose and virulence of
injected, and it is unlikely that harm would
injecting 0 01 mg of B C G into tuberculous
seems therefore possible to dispense with t
the B C G programme, using instead the
for testing sensitivity I suggest that an initi
of 0 01 mg be given intradermally over the
and that if no local reaction occurs in seventy
a vaccination dose of 0 1 mg be given at the
The multiple puncture technique might be
factory than the intradermal method The
test should be done with B C G of the stren
per ml and the subsequent vaccination w
per ml Ustvedt (1950) has found B C G too
determine sensitivity By adjusting the stre

the technique this difficulty might be over e very small dose of B C G would be harmless cted person while in the non infected there be time for sensitivity from the test injection before he was vaccinated Insufficient atten een given to Ustvedt s work on the diagnostic G The appearance of an accelerated reaction phenomenon would indicate tuberculous If no local reaction appears by the second testing it is highly probable that the person n tuberculous infection

fusion around the tuberculin test grows as ons proceed Palmer (1952) has stated that a le proportion of people giving a positive test have not been infected by the tubercle Conversely most of us have seen the patient ally active tuberculosis who reacts only to low of tuberculin The patch test is no longer is reliable Seibert and DuFour (1954) have the qualitative differences between O T and appears that the different antigens in the s exert their effects in people with different sensitivity

### GROUPS TO BE VACCINATED

orkers agree that contacts of known cases of is and those employed in hospital or clinic uld be offered B C G vaccination Young s are another group requiring protection But ut the newborn infant and the child up to of age ? In this group the need for vaccination ntirely on the incidence of infection in the area important that we do not vaccinate children rly for not only is the infant already subjected njections but mass B C G vaccination prevents f tuberculin testing for case finding and as an gnosis

mmunity where the prevalence of infection is the age of five years all possible protection rimary infection A including vaccination given to all children as the loss connected with rculin test is then of secondary importance d from the recent survey of Fisher (1954) ation under five years of age shows only 0 5% o tuberculin It is obviously unwise to vaccinate these children when the risk of becoming so small

rk of Gedde Dahl (1952) with tuberculin in a ng survey is well known and MacDougall 953) have shown how valuable this can be in Where the infection rate is low we cannot ay lightly such a useful method of finding active the vaccination were 100% protective and per t would be reasonable to suggest mass vaccina in a country where the incidence of infection is as this is not so I think that for the present ountry it is best to limit the vaccination of contacts The matter must be determined by ence of infection and the risk of developing berculosis

accination is only one of many means of pro e young child from tuberculosis Furthermore ants and very young children are vaccinated ction will gradually decline and unless reinfec place a state of vulnerability through dis ce of tuberculin allergy will ensue If the revert to tuberculin anergy the consequences serious to them particularly if they move to here they become exposed to virulent infection principle should control our vaccination policy ve reactor is likely to be exposed to tuberculous then he should be vaccinated with B C G This articularly to emigrants from areas where the rate is low to where this rate is high

### CONCLUSION

In the B C G vaccination programme there are certain limits of simplification beyond which at present it is unwise to go A pre vaccination test for allergy is necessary Segregation is still advisable where the risk of infection is great in the pre vaccination or post vaccination period Inspection of the local B C G lesion at the end of eight weeks is essential and the vaccinated should be tuberculin tested Special attention should be paid to those with a local lesion less than 4 mm in diameter Possibly the post vaccination test may be eliminated in the future, and with oral vaccination we may some day dispense with pre-vaccination testing but not before further knowledge has been obtained on the severity of Koch's phenomenon in relation to the type of vaccine and the method of administering it

The need for segregation has caused much discussion and one cannot do better than to repeat the advice given by the Ministry of Health—that segregation to prevent infection by virulent tubercle bacilli is desirable in the pre allergic period, but it is better to vaccinate without segregation than not to vaccinate at all Without segregation active tuberculosis will develop in a few cases shortly after vaccination but B C G vaccination schemes should not be prevented from developing because of this risk As a general rule the problem arises only in contacts and the risk should be assessed in each case Where there is likelihood of exposure to massive and frequent doses of tubercle bacilli during the vaccination programme then segregation is advisable for six weeks before, and six weeks after, the injection of B C G

## Timing of B C G Vaccination

If one tries to immunise a body simultaneously with two different antigens the formation of antibody to the inferior antigen may be considerably weaker than when immunisation is done with this antigen alone With the two antigens given at the same time one dominates the other This was shown by Doerr and Berger (cited by Refvem 1954) as early as 1922 It is therefore important to separate B C G vaccination from other immunological procedures so that tuberculin allergy may develop fully without any inhibition from other antigen antibody processes This applies particularly to smallpox vaccination which should be done first and separated from B C G vaccination by at least three weeks

In certain areas B C G vaccination has been suspended during outbreaks of poliomyelitis Instances have been reported in which poliomyelitis developed at the same time as the B C G lesion or shortly afterwards The circumstances have been investigated closely and there appears to be no reason to connect the poliomyelitis with the B C G vaccination

It would be unwise to vaccinate persons when recovering from measles or influenza owing to the depressing effect of these infections on tuberculin sensitivity

## Technique

The methods of B C G vaccination have been admirably described by Irvine (1949 1954)

One of the disadvantages is that it can be performed in at least four different ways These are (a) by oral administration (b) by multiple puncture (c) by scarification and (d) by intradermal injection

*Oral Administration*

This is the easiest method but outside South America it is not favoured because of the resulting low and short lived tuberculin-sensitivity This can be overcome by frequent periodic re-vaccination which calls however for close follow up of the vaccinated This method of vaccination has been little studied in Europe and it is high time that it was tested in this country If repeated vaccination by mouth proved successful how simple the whole procedure would become With the multiple puncture tuberculin test, we could eliminate all syringes, the rigid time schedule in the B C G programme, and the need for doctors to do the testing and vaccinating

From Brazil, de Assis (1953) reports that over 3 million persons have now been vaccinated by the oral technique 100 mg is given during the first week of life, followed by monthly doses of 100 mg for three to six months He claims that with this method a 100% conversion-rate is obtained and complications are rare, and that oral vaccination without tuberculin testing is harmless

Sayé (1953) administers B C G in a dose of 100–150 mg and repeats the dose every six months in non contacts In contacts he re-vaccinates for six months with the same dose every 8, 15, 28, or 90 days, according to the degree of exposure to infection

There is no reason to doubt that oral administration has given excellent results in Spain and South America, but there is evidence that the strain of B C G used in those countries is different from that used in northern European countries

*Scarification*

Scarification will give about 85% conversions It is difficult to obtain a higher rate, although the French claim 95% The method is slow, and a dressing has to be applied Complications are infrequent, but tuberculin-sensitivity develops more slowly than with the intradermal technique The results vary greatly, low conversion-rates are due to using too small quantities of vaccine or to too superficial scarification The method has the disadvantage that the amount of B C G introduced is unknown

*Multiple Puncture*

Rosenthal (1937) and Birkhaug (1947) have advocated vaccination by multiple puncture The method has the advantage of being particularly free from complications and local ulceration, but Geser (1954) has shown that the degree of tuberculin sensitivity obtained is less than by the intradermal method An advantage of this method is the absence of syringes and needles and the uniformity of operation The conversion-rate is satisfactory

The method has not been used much in this country, partly because a special strength of B C G is required (not less than 20 mg per ml ) and partly because of the expense and difficulty of obtaining the apparatus There is also the drawback of not knowing the amount of B C G introduced, but that is not of great consequence in routine work if the conversion rate is satisfactory and there are no complications The method deserves further investigation because of its simplicity and uniformity of operation

*Intradermal Injection*

An intradermal injection is not difficult to give, provided needles are sharp, syringes are good, and the subject keeps still The first two conditions can be satisfied, but children are liable to wriggle and infants can be difficult It is important that the injection is given intradermally Gaisford and Griffiths (1951) have shown that it is unnecessary to give a double dose to infants, and in Cardiff we have confirmed the experience of O'Meara and Price (1953) that the complication rate is greatly reduced by dividing the dose of B C G vaccine into two injections, each of 0 05 ml., into one arm In Cardiff we have been impressed by this technique and are adopting it for all children under the age of five years

It is somewhat unfortunate that there are four methods of vaccination, each requiring its own particular strength of vaccine There is little doubt that the incidence of complications and the degree of tuberculin sensitivity are related to the manner by which the B C G is given In Great Britain we favour the intradermal technique, he multiple puncture method could be made to produce more permanent tubercul be the method of choice since it is performed than any other The disadvantage dose of B C G is unknown, but if the carefully used it is doubtful whether the much greater than by the intradermal te

### FUTURE TRENDS

I have mentioned these methods because in the future there must be considerable of the B C G programme In the years to infection will become very much less age groups The herd immunity will con Tuberculosis may then become an acute disease, particularly in young children and But there will always be a hard core of infection lesions that can infect the majority For these B C G will be the herd immunity The freeze dried ultimately be the type generally used. all routine vaccination, the multiple- culin test will, I think, replace the one, but ultimately a tuberculin test be required at all Multiple puncture be favoured. Post-vaccination tuberculin I think, be restricted to those who fail to reaction of a certain degree of intensity It improbable that newborns and infants will vaccinated by the oral technique, as Sayé (1953) These changes will, I think, of the present disadvantages of B C G

## Complications

The most serious complication of seminated tuberculosis In two published 1954, Thrap-Meyer 1954) death has followed nation, and a third death, in Sweden, has been There has been no explanation of these results, except that the patients had no inherent to the infection This is not the complete of the patients was not healthy, since he increased erythrocyte sedimentation rate for vaccination Further information is needed causing this failure of the defence mechanism

Fortunately, serious complications are Minor complications are commoner than can be troublesome for many months associated with their development, would mention (*a*) the inherent individual, (*b*) the potency of the vaccine magnitude of the dose, and (*d*) faulty techn

From a study of reports on complications sent to the Ministry of Health up to the certain impressions have been gained The no statistical value since the total number of tions and of vaccinations is not known of the reported complications arose in 1951 the reported number fell considerably in of course, may be because of a decline in reporting, but I prefer to believe that imp technique had an influence Complications batch of vaccine were rarely reported from places This means that generally the factory Certain isolated ampoules may considerably in strength from the majority but this was difficult to prove

The *age distribution* of the 250 cases with was as follows up to one month, 157, two to seven to twelve months, 14, one to two years, five years, 14, six to ten years, 7, eleven to fi sixteen to twenty years, 8, twenty one to twenty Thus complications were commoner in the young This may be due to faulty technique, but more is due to low resistance of the tissues

ME OF SINUSES IN 166 CASES ACCORDING TO AGE

| No of cases | Healing time (mos) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | −2 | −3 | −4 | −5 | −6 | −7 | −9 | −12 | Over 1 |
| 116 | 1 | 9 | 14 | 7 | 15 | 4 | 24 | 31 | 8 |
| 22 | | 3 | 2 | | 1 | 3 | 9 | 5 | |
| 10 | | 1 | 2 | 2 | | 1 | | 2 | 9 |
| 5 | | | 1 | | | | 1 | 3 | |
| 5 | | | | 1 | 1 | | | [illegible] | 1 |
| 6 | | 1 | 1 | | 1 | 1 | 1 | | 1 |
| 2 | | 1 | | | | | 1 | | |

*odes* were involved as follows inguinal 94 09 cervical, 15 hilar 8; multiple 2 site not Calcification was recorded in 20 cases

*mplications* were as follows lung infiltration, 4 ar conjunctivitis, 3; erythema nodosum, 2; late itis 2; implantation ulcer 2 joint pains, 3 skin rash 2; lupus 1

*nt*—Where this was recorded lymph node involve- as follows: local streptomycin injections 32; ular streptomycin 4; local *p*-aminosalicylic acid oral P.A.S 14 aspiration only 22; ultra t, 13; excision, 10 incision and curetting 3; 1; penicillin, 5; silver nitrate 2; dry dressing 24

*ing-times* in months in 166 cases with sinuses, were : up to two 1 three to four 34 five to six 31; ight, 37 nine to ten 31 eleven to twelve 20 fourteen, 0; fifteen to sixteen 9; seventeen to 0; over eighteen 3 The healing times according of the patients are shown in the accompanying

ases *acid fast bacilli* were sought and in 35 found hese 35 cases the bacilli were typed and were found e character of B C G

figures show a high preponderance of complica infants, long persistence of sinuses in some d diversity in treatment

## Conversion and Reversion

he improved technique it is usual for at least hose vaccinated to show tuberculin allergy six weeks after vaccination Over 80% are allergic eks after injection with fresh B C G but post on sensitivity is not maximal until eight weeks sed Frew (1954) has shown that some degree ulin-sensitivity is present before the local B C G velops which would mean that the development G lesion at the site of inoculation is due to the f the bacillus by the sensitivity that is develop th freeze dried vaccine, it may require three o reach maximum allergy These periods are t since it is desirable not to return a person or low, tuberculin-sensitivity to an infectious ment *If the vaccinated persons are exposed to* infection, the sensitivity conferred by B C G will ented by that following subsequent infections rsely populated area or a country with a low rate this may not occur The person will then rely for protection on the permanency of the lergy It is therefore important to know how asts. There are records of its disappearing as six months and lasting as long as seven years past two years we have been finding in Cardiff reversion rate after the first year was 10% for vaccine and 15% for the dried at the end of d year the corresponding figures were 20% and Ve always re tested on the left arm, where the tuberculin test had been done. Because of the ersion rate Dr Phyllis Bowen began this year t on both arms and she found that a year after ion some vaccinated children were negative eft arm and positive on the right arm Now e testing always on the opposite arm to the one previous tuberculin testing was done and our reversion rate has fallen to about 2% The observatio is important for although it is well known that a loc desensitisation to tuberculoprotein *develops for a sho* time at the site of tuberculin testing I do not think is generally realised that this desensitisation extends t two or three inches from the site and can persist for a least twelve months

The lesson is: always re test on the arm that wa not previously used for tuberculin testing Unfortunatel we have only two arms so I am at a loss to know wha we do in a three or four year follow up Possibly w shall have to go to the lower limb or possibly sensitivit is regained after two years. Certainly more work i needed on this interesting phenomenon

## Records

It may be wrong to mention the need for keepin records as a disadvantage of B C G vaccination, but it i most important that records be kept particularly i regard to young children Without records the tuberculin sensitivity resulting from B C G vaccination may b ascribed to virulent bacilli and lead to a diagnosis o active tuberculosis This has already occurred, and wi occur again if the physician examining the patient i not informed of the vaccination Furthermore, fo administrative purposes it is necessary to know th number of those vaccinated, and epidemiologically it i useful to know the number of vaccinated persons wh develop tuberculosis It is therefore essential to kee good records

In B C G work *record keeping falls into three categorie*

1 There are the official statistics required by the Ministr of Health The minimum required are those needed t determine the number vaccinated It would be an advantag if it were always made clear that a particular child had bee *vaccinated and some local authorities have instituted* vaccination certificate But at present some physicians ar vaccinating without informing the chest physician or th medical officer of health this is unfortunate and should b rectified as soon as possible

2 There are the records required by special investigation established for a specific purpose by an official body an backed by funds and personnel.

3 There are the records required for personal survey organised by one or more persons to throw light on som particular aspect of B C G vaccination

In all these records it is essential to maintain sim plicity and refrain from investigating too many aspect of the problem at once It is essential that the vaccinatio programme in any area should not expand faster tha *the recording system can deal with the returns*

A simple record card well kept is better than a complicated one kept badly Much will depend on th nature of the investigation but perhaps the controllin factor is the number and training of the staff who wil be called upon to keep the records

## Finale

Perhaps the greatest disadvantage associated wit B C G vaccination is the unwarranted confidence that it has inspired in laymen in many countries; many believ that it is a complete protection against tuberculos This can easily lead to the neglect of essential measure for eliminating the predisposing causes of tuberculosi and the spread of infection

B C G is an important pillar in the structure of our preventive services but it cannot stand alone

I am grateful to Dr Phyllis Bowen, of the B.C.G Clini Cardiff for permission to describe her unpublished work

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*References continued overleaf*

# URINARY EXCRETION OF ŒSTROGENS DURING THE MENSTRUAL CYCLE

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Many workers have measured the excretion of œstrogens in the urine during different phases of the menstrual cycle The most constant finding has been two peaks of excretion, one about the time of ovulation and the other during the luteal phase However, most of the results have been obtained using bio assay methods and have been expressed in terms of animal units of total œstrogenic activity (see Gustavson et al 1938, Pedersen-Bjergaard and Tonnesen 1948) Since at least three œstrogens (œstriol, œstrone, and œstradiol-17β) have been found in human urine, and it is erroneous to measure biologically such a mixture of substances, activities, the results obtained have litt significance Smith et al (1938) and Smit (1952) obtained more reliable results by s œstrogens, before bio assay, into œstriol, œstradiol fractions, and expressing their res of the weights of pure crystalline œstrogens

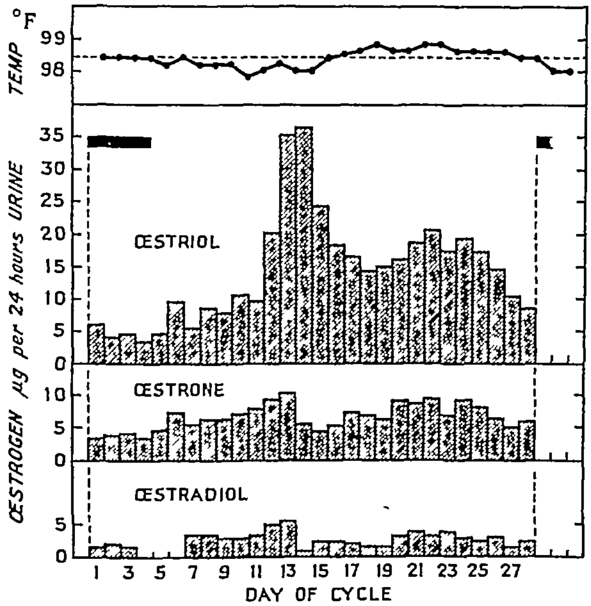

**Fig 1—Subject 1, aged 36 para.-3 This figure and figs 2–8 show the amounts of œstriol, œstrone, and œstradiol excreted per 24 hours, and also the variations in basal temperature ▬ = Menstrual period**

Jayle and Crèpy (1952) used the Kober re to measure total œstrogens and reported obtained throughout two menstrual cycle figures, too, have limited quantitative m œstriol, œstrone, and œstradiol 17β all g colour intensities in the Kober reaction. E Engel et al (1950), and Migeon (1953) at

*ŒSTROGEN LEVELS FOUND AT VARIOUS TIMES*
MENSTRUAL CYCLE
(Collected from ten cycles)

| Time in cycle | Œstrogens excreted (µg per | | | | |
|---|---|---|---|---|---|
| | Average | | | | |
| | Œstriol | Œstrone | Œstradiol | Œstriol | Œ |
| Onset of menstruation | 6 | 5 | 2 | 0–15 | 1 |
| Ovulation peak | 27 | 20 | 9 | 13–54 | 11 |
| Luteal maximum | 22 | 14 | 7 | 8–[illegible] | 10 |

measure the urinary œstrogens excreted menstrual cycle by using counter current to separate and identify the individual fluorimetry to measure them However, contaminants interfered considerably with th ment of œstrogens, and the main significance was that Migeon obtained good evidence th œstrone, and œstradiol are all present in pool cycle urine

More recently a convenient, accurate, and specific chemical method for separately œstriol, œstrone, and œstradiol 17β in huma been developed (Brown 1955a and b), and it i

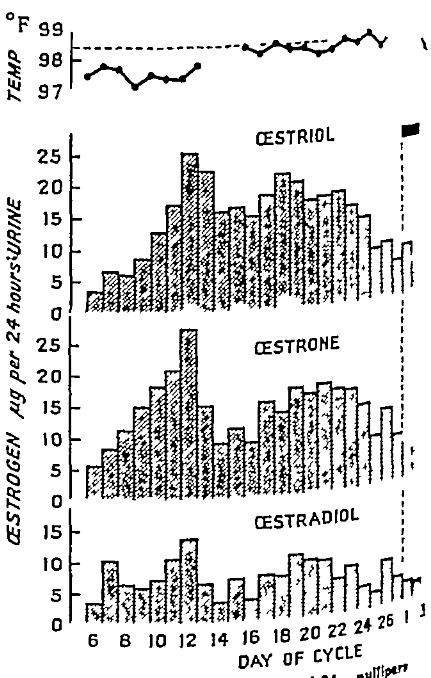

**Fig 2—Subject 2 aged 34, nullipar**

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more reliable and detailed measurements of tion I report here the results of applying this a study of the urinary excretion of œstrogens number of menstrual cycles of apparently men This was a necessary preliminary to the abnormal conditions A preliminary com on some of these results has already been (Brown 1955a)

## Method

e 24 hour urine specimens were collected daily le whole menstrual cycle of eight apparently men whose ages ranged from 17 to 40 years es (subjects 7 and 8) two whole menstrual cycles ied The amounts of œstriol, œstrone and 17β in each 24 hour urine specimen were d by the chemical method described by Brown Morning basal temperatures were taken orally t each cycle to correlate the œstrogen levels of expected ovulation

## Results

ults are shown in figs 1 to 8 and in the both cases where two cycles were studied the

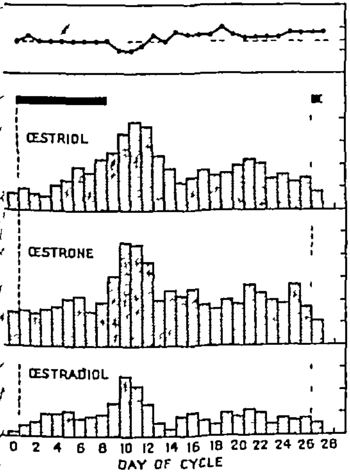

Fig 3—Subject 3 ; aged 40 ; nullipara.

tained during the second cycle of each individual st identical with those obtained during the first onsequently only one cycle from each subject is in the figures

ber of features common to all the cycles is The amounts of the three œstrogens excreted rise and fall together The œstradiol levels are lways lower than the corresponding œstrone o ratio between the two being approximately at 1 2 There is no such constant ratio between ol and œstrone levels for the œstriol level may to or greater than the corresponding œstrone he amounts excreted are lowest during the first the cycle and begin to rise at about the 7th day a well-defined maximum (the ovulation peak') the 13th day—or, more accurately 14 days he onset of the next menstrual period This n occurs about the time of the temperature rise resumably related to ovulation The peak is by a sudden decrease in œstrogen excretion

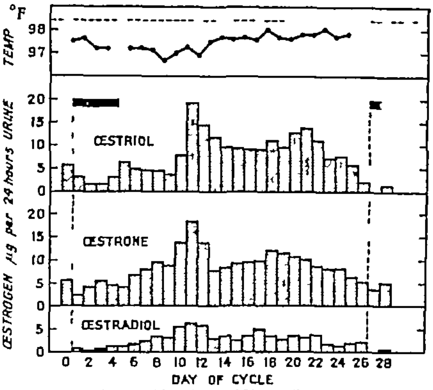

Fig 4—Subject 4 ; aged 28 ; nullipara.

During this phase of the cycle the changes in the œstrone and œstradiol levels parallel one another but the changes in the œstriol levels tend to lag about 24 hours behind the other two This lag phenomenon is sometimes masked by the 24-hour interval over which the urine specimen is collected but even so is clearly seen at the time of the ovulation peak and subsequent drop After suddenly decreasing the œstrogen levels tend to increase again to a second maximum (the 'luteal maximum'), which occurs on about the 21st day and then decrease before the onset of menstruation During the luteal phase the œstriol lag is not apparent The lowest levels are often reached several days after the onset of menstruation

While the pattern of œstrogen excretion is constant the actual amounts found in the urine of different subjects vary over a considerable range. Those found at the onset of menstruation at the ovulation peak and at the luteal maximum are summarised in the table.

No abnormal symptoms were recorded by any subject during the cycle studied Furthermore three subjects (4 7 and 8) two of whom (7 and 8) were still collecting urine for assay became pregnant shortly afterwards and a parous subject whose œstrogen excretion was similar to that of subject 6 became pregnant during the cycle being studied There is therefore no evidence of correlation between the relative or absolute amounts of œstrogens excreted and the subjective symptoms parity or fertility of the woman On the other hand it is interesting to note that the youngest subject (5) excreted the lowest amounts of œstrogens

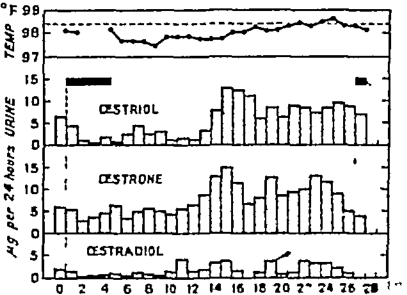

Fig 5—Subject 5 ; aged 17 ; nullipara

## Discussion

The results reported here show two peaks of œstrogen excretion during the menstrual cycle, and in this respect are similar to those reported by other workers. Quantitatively, too, they are similar to those reported by Smith et al (1938) and Smith and Smith (1952). They present, however, a more detailed picture of some of the events which occur during the menstrual cycle. We see, for instance, that the rise to the ovulation peak is usually gradual, and the most satisfactory explanation for this is an increasing production (and secretion into the blood) of œstrogen from a rapidly enlarging follicle, rather than a sudden release of œstrogen rich follicular fluid at ovulation. At the peak itself both factors may operate. The highly characteristic ovulation peak was a constant finding in all the normal cycles studied. Since neither ovulation peak nor luteal rise have yet been observed in this laboratory in any woman having a uterus and suffering from amenorrhœa, the finding of such a peak may be good evidence of the occurrence and time of ovulation. The pattern of the three œstrogens about the time of ovulation—namely, œstradiol levels about half the œstrone levels, and the œstriol levels lagging a day behind—is essentially similar to that observed after the intramuscular injection of œstradiol 17β (Brown 1955a). This furnishes further support for the generally accepted view that œstradiol 17β is the primary ovarian hormone at this time. The sudden decrease in œstrogen excretion after the ovulation peak could be due to a sudden change in follicular function by rupture at ovulation. If this is so, the drop in œstrone and œstradiol levels should follow very closely and indicate its time more the temperature rise, which seems to depend gradual and variable increase in progesterone, which also takes place at this time (Davis and The luteal maximum is probably due t produced by a growing and then regre luteum. One possible explanation for th absence of the œstriol lag at this time œstriol and œstradiol 17β may be produ corpus luteum, and that the urinary œstriol fore be derived directly from the corpus as from the normal metabolism of œstradiol-

Since, unless the circumstances are exce day-to day variation in œstrogen excretion more important than the amounts excreted time, single random estimates of urinary women during reproductive life will have cance unless the specimen has been collected a and accurately known time in the cycle. Seria

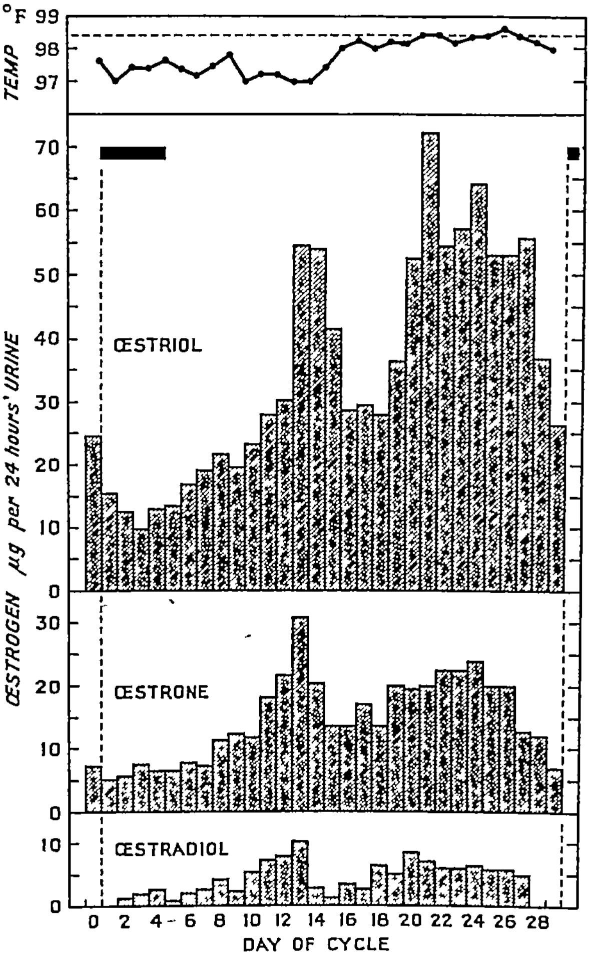

Fig 6—Subject 6 aged 32 para 2.

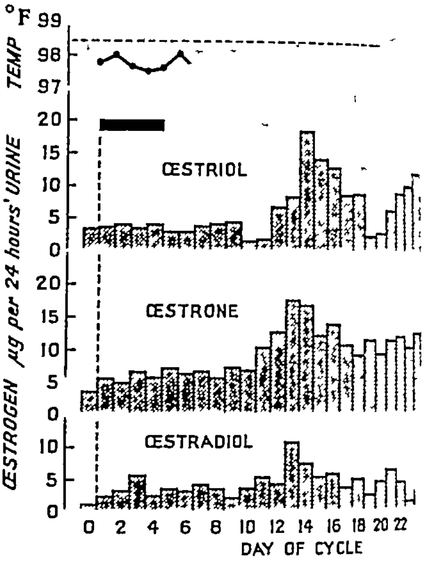

Fig 7—Subject 7, aged 33, para-1

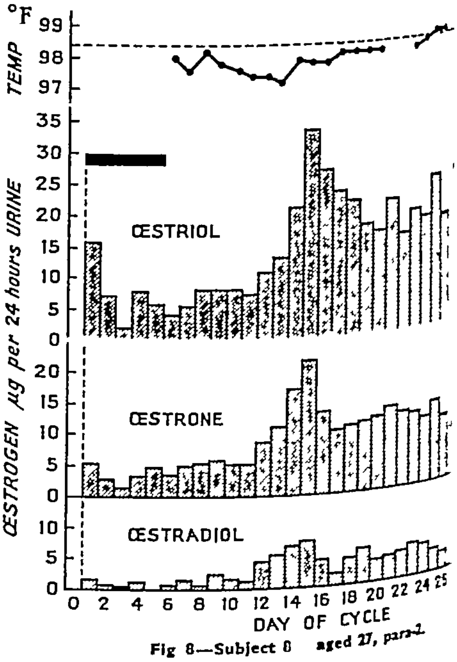

Fig 8—Subject 8 aged 27, para-1

be necessary before any accurate assessment of notion can be made employing these methods.

## Summary

obtained using a new chemical method for ; the urinary excretion of oestriol oestrone, and 17β during 10 normal menstrual cycles in e recorded and discussed

o thank Prof. G F Marrian F.R.S and Prof R J their interest in this work I am also grateful le members of the staff and wives of colleagues who l the specimens and to Mr H A. F Blair and Miss kie for their skilled technical assistance

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# ECTIVE CIRCULATION OF THE INE WALL IN LATE PREGNANCY

## MEASURED WITH $^{24}$NaCl

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eais that pre-eclampsia might be associated cental ischaemia led Browne and Veall (1953) pt the measurement of placental blood flow isotope technique they were able to locate the n women during the last trimester of pregnancy ts in whom the placenta was placed anteriorly cted isotonic saline solution containing $^{24}$NaCl he uterine wall into the placenta. Browne and wed that the rate at which the injected material ved from the placental site varied considerably , tensive women the removal was extremely rapid in patients with raised blood pressure either eclampsia or from essential hypertension it was lelayed

minished clearance rate might result from inade elopment of or from pathological changes within nta itself or from a reduction of the blood om the uterine wall To elucidate this question of value to attempt comparative measurements (as opposed to placental) blood flow in normal e-eclamptic pregnancies

## Method

present series of observations 0 3–0 4 ml of aline solution containing $^{24}$NaCl with an activity μC was injected directly into the uterine wall ndard procedure the area chosen was the lower rant, about 4 cm below and to the side of the umbilicus The abdominal wall and peritoneum were locally infiltrated with 1% lignocaine hydrochloride ( Xylocaine ) and the injection needle was introduced through the anæsthetised area It was possible to ascertain when the needle had been inserted into the uterine wall because the abdominal muscles moved relatively more than the uterus when the woman took a deep breath this caused the needle head to be deflected sharply downwards When the needle was properly positioned neither blood nor liquor amnii was withdrawn by suction on the syringe

In every case the nature and main features of the investigation were explained to the patient before the examination was started. Their most frequent reaction was one of interest and willingness to coöperate The procedure caused them very little inconvenience They felt only the introduction of the local anæsthetic through the skin and later a very transient, sharp, and deeply located prick when the uterine peritoneum was pierced Many of them said they felt nothing

The injection of the radio sodium was made as rapidly as possible Care was taken to prevent leakage along the needle track by emptying the syringe while the needle was fully inserted the skin was wiped free from blood and saline solution after the needle had been withdrawn A screened end window γ ray Geiger Müller counter was immediately placed over the site of the injection and to maintain its position relatively constant, fixed to the skin with adhesive tape During the period of observation the counting rates over the injection site were recorded at $^1/_2$ minute intervals on a counting rate meter The results were expressed as the ' time to half value ' after a correction had been made for the rising background caused by an increasing amount of $^{24}$Na appearing in the blood stream after its removal from the injection pool This corrected counting rate $(c-b)$ was calculated for each observed counting rate $(c)$ from the following formula

$$c-b=c-\frac{b_1(I-b_1)-c(b_2-b_1)}{I-b_2}$$

where $I$ = initial count per min $b$ = corrected background count per min $b_1$ = initial background count per min $b_2$ = final background count per min and $c$ = observed counting rate to be corrected for background The final background $(b_2)$ was obtained by observing the counting rate over the contralateral area of the uterus at the end of the experiment For this purpose it was assumed that this count represented the radioactivity in a cone of tissue corresponding to that containing the injection site but free from radiations arising from the residual pool of the radioactive material

This technique was essentially similar to that described by Kety (1948 1949) to measure the clearance rate of locally injected radioactive sodium from the site of injection Though such clearance depends on many interacting factors (McGirr 1952) it is essentially based upon the postulate that the rate of removal of a diffusable substance is proportional to and offers a measurement of local tissue circulation It must however be emphasised that the technique measures the *effectiveness* of local tissue circulation rather than the absolute blood flow in the area

In the present study certain factors which influence the clearance rate of the injected sodium may be considered to be uniform Thus the temperature of the uterine wall may be assumed to be independent of environmental conditions since the patient is confined to bed moreover the restricted skeletal muscle activity which is possible can have little influence on the uterine blood flow Finally the uniformity of texture of the unstriped musculature of this organ renders it improbable that spurious results will arise from leakage of the tracer substance from the site of injection along fascial layers.

On the other hand, certain uncontrollable factors may considerably influence the clearance rate of $^{24}$NaCl from the wall of the uterus Of these the chief are (1) the effects of rhythmic uterine contractions, (2) the tonicity of the musculature, (3) the proximity of the injection site to the placenta, and (4) the depth of the injection from the peritoneal surface of the uterine wall In this preliminary study no attempt was made to assess the influence of these factors on the clearance-rate of the injected material Repeat observations on individual patients, however, were satisfactorily comparable In 9 instances where repeated measurements were made the differences between the observed clearance times were never greater than 0 7 minute There was, therefore, no indication that the unknown variables were interfering with the reliability of the observed results

## Material

Observations on the clearance-rate of radio sodium from uterine muscle were made on 48 pregnant women Of these, 20 were normal uncomplicated cases between the 34th week of pregnancy and term Half of these women were primigravidæ, 6 had had one child, and only 4 had had several pregnancies The criteria of normality were their general obstetrical condition coupled with normotension—i e , a diastolic pressure consistently below 85 mm Hg

A second and smaller group of 10 cases were classed as mild pre eclampsia These women had been admitted to hospital because of a sudden rise in blood-pressure with or without albuminuria The diastolic pressure of this group was 85–95 mm Hg Observations were again made between the 34th week of pregnancy and term In this group 6 women were primigravidæ, 3 had had one child, and 1 only had had several pregnancies

We examined a small group of 8 cases of severe pre-eclampsia In these the diastolic blood-pressure was 95–115 mm Hg, and all these women showed typical signs of pre eclampsia The period of gestation in these women was somewhat shorter than in the other two groups , the observations were made between the 30th and the 39th weeks of pregnancy Of these 8 women, 4 were primigravidæ, 1 had had one pregnancy, and 3 had had several pregnancies

Finally, we examined a series of twin conceptions At the time of investigation the infants were viable and apparently normal, though in 1 case the fœtuses died before delivery These women were observed between the 32nd week of gestation and term Six were primigravidæ, 3 had had one pregnancy, and only 1 had had several pregnancies

## Results

The average clearance rates of $^{24}$NaCl from the uterine muscle, together with the standard errors of these means, are set out in the accompanying table for the four groups of women examined

AVERAGE CLEARANCE RATES

| Type of pregnancy | No of observations | Time to half value (min.) |
|---|---|---|
| Normal | 20 | 4 1 ±0 354 |
| Mild pre-eclamptic | 10 | 7 7 ±0 523 |
| Severe pre eclamptic | 8 | 15 3 ±2 854 |
| Twin conception | 10 | 6 6 ±1 054 |

It is evident from these figures that the clearance rate of the injected diffusable ion is greatly reduced in pre eclampsia In the mild cases, where the diastolic blood-pressure had never risen above 95 mm Hg, the average clearance time was about twice as long as in the normal controls In the severe cases this prolongation of clearance time was even greater, the average being almost four times that of the normal Examined statistically by the Fisher method for small sampl exhibited strongly significant differences less than 0 01 both between the normal mild pre eclamptics and also between the m cases

Similarly there was a significant difference normal single pregnancies and the twin being less than 0 01, which implies a chance 100 to 1 that the means of the groups are

## Discussion

From a consideration of the functions of circulation two salient points emerge. Fir supply, through the placenta, the metabolic growing fœtus, and this demand probably h others Secondly, it must also maintain th integrity of the trophoblast It is possible th circumstances, the uterine circulation m sufficient for the former but inadequate for t

From the study of severe early pre-e constant findings appear (1) its onset is extremely sudden and the hypertension and (2) the placenta is almost always ver seemingly underdeveloped, and of poor fun the trophoblast, by reason of its unique function and activity, has a high oxygen Many of the biochemical changes known to pre eclampsia, such as the diminished pro œstrogen activity (Smith and Smith 1948), the in adrenocortical secretion (Venning et al. 19 production of histaminase (Ahlmark 1944), impairment in the trophoblastic metabolis findings suggest that the pre eclamptic becomes manifest at a time when the fœtus, together with those of the tropho the supply that can be maintained by th circulation, and it is possible that trophoblas may prove to be an important factor or even mechanism " which determines the ons eclampsia Although the fœtus in these ca in utero for a few weeks, its development retarded and it remains grossly undersized. the maternal blood flow may have been to fulfil its dual function to the fœtus trophoblast

The hypothesis that a reduction in blo the uterus is a factor in the onset of pre-ec received considerable support (Page 1939, 1946, 1948, Bastiaanse and Mastboom 19 workers have emphasised that the incid eclampsia is particularly high in twin hydramnios, essential benign hypertension, tidiform mole In each of these conditions th cumstances which could lead to a relative fa effective circulation and consequently to tr anoxæmia

From our results it appears certain that significant reduction in the effective uterine associated with pre eclampsia which dev previously normotensive woman This r probably one of the main factors responsi decreased placental flow described by Brown (1953) The reduction in flow appears to related to the increase in diastolic blood is interesting that, from our observations, an 10 mm Hg is associated with a clearance ra at best, only half that of the normal, whereas severe cases the effective blood flow is o fraction of the normal

We have had no opportunity to study clearance-rate before and after the onset of Nevertheless the results in our small series of cated twin pregnancies, which are recogni particularly liable to develop pre-eclampsia,

blood flow is not so adequate in them as in the
This is also true of our scattered observations
with hydramnios and preconceptional hyper
All these show clearance rates which fall at
limit of normality and could therefore be
to be on the verge of pre-eclampsia
bed is a well-established therapeutic measure
ment of pre-eclampsia and often brings about a
fall in blood pressure In recent years severe
also been treated with various hypotensive
h as hexamethonium (Morris 1953) hydra
lazine (Assali and Suyemoto 1952) and
veratrum (Meilman 1953 Käser 1954) and of
There has been some debate about the value
eatment and it has been suggested that the
potension may perhaps only be masking and
ating, the underlying pathological changes
e course of the present study it has been
make observations on 5 patients with severe
sia both initially and later when effective
o treatment had been initiated. In these
e initial uterine clearance rate was extremely
after therapy with a hypotensive drug there
old or threefold increase which coincided with
ion of the blood pressure
bservations appear to confirm that the use of
is of demonstrable therapeutic value It is
at any *measure which increases uterine* and
ental, nutrition must be advantageous to the
nt of the fœtus The ultimate success of such
however depends on the capacity of the
for if this organ is already grossly infarcted
veloped it may still fail to sustain fœtal life
55) even though the blood flow in the uterine
stored to normal

## Summary

d for the measurement of effective blood flow
ine wall during pregnancy is described using
nce-rate technique
tions of the effective flow between the 30th
estation and term were made on 20 normo
men, 10 normal twin pregnancies and 10 mild
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ompared with that in normal single pregnancy
ctive flow was about half the normal in mild,
quarter the normal in severe cases of pre-

ments suggest that therapy with hypotensive
severe pre-eclampsia increases the effective
in the uterine wall

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# ACTION OF BREATHING EXERCISES IN PULMONARY EMPHYSEMA

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Breathing exercises are often used as a treatment for pulmonary emphysema Most patients believe that they are helped by them The popularity of this treatment appears to depend on its subjective effect alone, since we have been unable to find any published reports of an objective assessment of its value

The work we report here was designed as a preliminary to an examination of the long term effects of breathing exercises Its aim was to investigate the performance of the exercises and their mode of action on respiration so that the benefit attributed to them could be judged objectively their technique and theoretical aims examined critically and if possible, the manner of performing the exercises improved

We use the words immediate action to describe *the changes which take place* when the *patient is performing* breathing exercises The word effect " is used to denote changes which take place as a result of the patient having practised the exercises over a period of time We have been concerned primarily with the immediate action ' of the exercises but we have also some results of their ' effects "

## Material

Ventilatory function was studied in 12 emphysematous men before and after a course of instruction in breathing exercises These patients had been tested repeatedly from the winter or spring of 1953 until the summer of that year and the results of that prolonged observation have been published (Friend 1954)

Electromyographic examinations were made on 7 of these 12 patients before and after instruction in breathing exercises These studies before exercises were made in the summer months when the patients had become accustomed to spirometry They were repeated within two months of completing instruction in the exercises In addition cases 14–16 were examined before exercises but they failed to attend for the exercises

## Methods

### *Ventilatory Function*

The *total lung capacity and its subdivisions* the mixing efficiency and the size of the poorly ventilated space were determined by the closed-circuit method using helium as the indicator gas The maximum breathing capacity was measured with a spirometer of the type described by Bernstein et al (1952) The effective tidal volume was calculated from Briscoe's (1952) formula which applies to the mixing of inert helium inspired into the lungs and not to the measurement of the effective tidal volume from expired and alveolar air concentrations of oxygen or of carbon dioxide.

Allowance was made for an increase in the spirometer circuit and a decrease in the *functional residual capacity* when patients, performing breathing exercises began the test by exhaling into the spirometer instead of as is usual inhaling from it

After instruction in breathing exercises the tests were repeated, usually on several occasions, all observations except the vital capacity and maximum breathing capacity being made when the patient breathed naturally and also when as taught

*Electromyography*

Recordings were taken from the sternomastoid, rectus abdominis, and external oblique muscles by the technique described by Campbell and Green (1953a) These muscles were used for the following reasons (1) they are all easy to study with surface electrodes, (2) the sternomastoid is a well-isolated muscle of inspiration and is used only at high levels of ventilation in healthy people (Campbell 1954) (other inspiratory muscles, such as the scaleni and the intercostals, vary considerably in their activity and may be active during quiet breathing in some healthy people), and (3) the anterolateral abdominal muscles are the only muscles of expiration in which surface electrodes detect activity during increased pulmonary ventilation Activity in intercostal muscles, even when they contract, is slight and occurs later than it does in the abdominal muscles (Campbell 1954) The abdominal muscles come into action towards the end of expiration rather than at its beginning Activity of these muscles during or at the end of inspiration is uncommon in healthy people during increased pulmonary ventilation It occurs regularly, however, at the end of an isolated maximum inspiration (Mills 1950, Campbell 1952, Campbell and Green 1953b)

The following tests were made on all 10 patients

(1) Quiet breathing without spirometry

(2) The effects of skeletal movements, such as raising the head from the couch and moving the trunk. This was done to find the electrical activity associated with slight and with vigorous contractions of the muscles

(3) Records were taken when the patients made voluntary maximal expiratory efforts so that their activity in these circumstances could be compared with that obtained by the breathing exercises

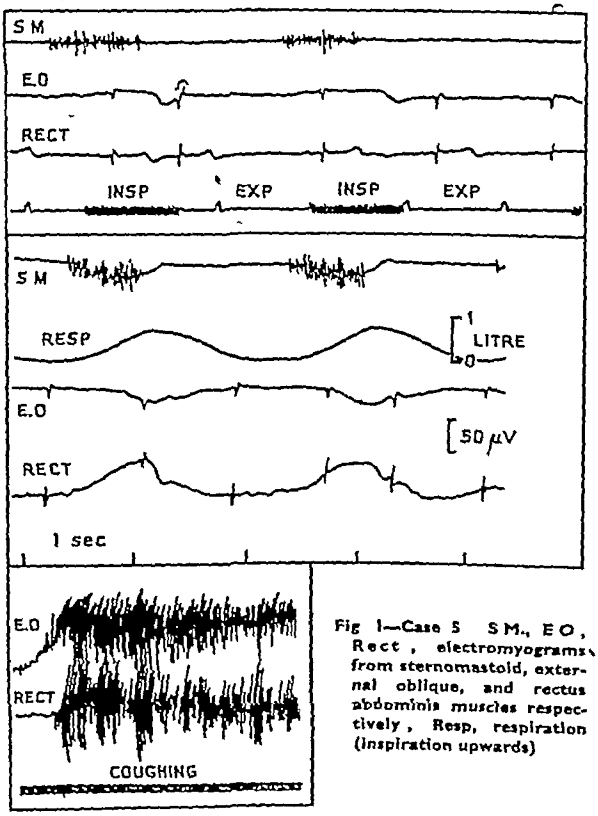

Fig 1—Case 5 S M., E O, Rect, electromyograms from sternomastoid, external oblique, and rectus abdominis muscles respectively, Resp, respiration (inspiration upwards)

A, breathing without spirometry rhythmic inspiratory activity in sternomastoid but no detectable activity in abdominal muscles.

B, after severe exercise when patient was intensely dyspnœic no expiratory activity in abdominal muscles

C during mild voluntary cough (amplification and time as in A and B) much activity of abdominal muscles

TABLE I—MEAN RESULTS OF VENTILATORY
BEFORE BREATHING EXERCISES

| — | Me |
|---|---|
| Age (yr ) | [illegible] |
| Total lung capacity | [illegible] |
| Vital capacity | [illegible] |
| Inspiratory capacity | [illegible] |
| Expiratory reserve volume | [illegible] |
| Residual volume | [illegible] |
| R V /T L C (%) | [illegible] |
| Mixing efficiency (%) | [illegible] |
| Poorly ventilated space/functional residual capacity (%) | [illegible] |
| Maximum breathing capacity (litres per min ) | [illegible] |

All volumes corrected to 37°C and recorded to

(4) Rebreathing expired air from the spirom CO$_2$ absorber removed so that pulmonary venti The patients were told that they would gradual to "breathe harder," and that they should try let this take place until they could no longe discomfort After one or two attempts the records showing smoothly increasing

In addition, 3 patients were examined ately after running on the spot to the limit to find the extent to which abdominal mus then to aid expiration

In those patients who were re examined af been taught breathing exercises the repeated during natural breathing and whil was instructed to "breathe as you were

All the manœuvres were repeated severa the patterns of activity described were reproducible The values recorded for th ventilation were the largest attained by The main study was made with the pa because there is a liability to postural activi and trunk muscles when the patient is made the detection of respiratory variation Observations made in the erect posture we similar to those recorded with the patient nothing was found to suggest that the muscular pattern of breathing varied with

*Breathing Exercises*

These were taught to the patients individ three times each week for from four to six were of the type described by Reed (195 (1953) and appear to be those commonly workers suggested that the exercises would following aims, which we have taken objective examination

(1) The attainment of relaxation of the muscl those of the neck and upper thorax

(2) The prolongation of expiration obtained the patient to breathe slowly out while count and then to inhale during a count of two

(3) The development of diaphragmatic move lowering of the costal margins by contraction abdominal muscles

(4) The inculcation of a habit of controlled The exercises were taught initially with the pa progressed to the patient performing them sitt and finally walking The physiotherapists were all our patients performed the exercises satisf end of their period of instruction

## Results

### BEFORE BREATHING EXERCISES

*Ventilatory Function*

In table I are the detailed results of the on the patients in June–August The formed an abnormally large proportion of th capacity, the mixing efficiency was reduced was a large poorly ventilated space in all maximum breathing capacity in every pat

, of the mean result in 11 healthy men aged e, studied by one of us (J F)

*ography*

—voluntary skeletal movements caused definite activity There was much activity in the l muscles of all the patients tested on voluntary and coughing (fig 1c)

ults are set out in table II Of the 10 patients 6 sternomastoid muscle during the inspiratory quiet breathing The sternomastoid was in use patients when their pulmonary ventilation was by rebreathing expired air No patient how d the abdominal muscles to aid expiration uet breathing (fig 1a) and only 2 of the 10 muscles when their ventilation had increased breathing

its were examined immediately after they had to their limit of tolerance Only 1 of them used inal muscles during expiration

DURING BREATHING EXERCISES

*y Function*

ults of pairs of tests taken on the same day the patient was breathing naturally and the ng breathing exercises are shown in table III a spirometric tracing from case 5 shows two natural breathing with a three minute period

MUSCULAR ACTIVITY SHOWN BY ELECTROMYOGRAPHY ORE INSTRUCTION IN BREATHING EXERCISES

| At rest | | Rebreathing expired air | | After exercise Abd muscles on expiration | Pulmonary ventilation on rebreathing expired air (litres per min.) |
|---|---|---|---|---|---|
| rno toid m pira on | Abd muscles on expiration | Sterno-mastoid on inspiration | Abd muscles on expiration | | |
| + | − | + | − | | 22 5 |
| + | − | + | − | − | 21·0 |
| − | − | + | − | | [illegible]2 0 |
| + | − | + | + | | 24 0 |
| − | − | + | + | + | [illegible]7·0 |
| + | − | + | − | − | 11 0 |
| − | − | + | − | | 29·0 |
| | − | + | − | | 26 0 |
| + | − | + | − | | 8 5 |
| + | − | + | − | | 3·0 |

ng exercises between them As in most of the tudied, respiration during the exercises was entirely below the normal resting respiratory n increased depth and at a slower rate The idal volume was more than balanced by the respiratory rate hence in 10 of the patients volume was smaller during the exercises than tural breathing Some patients could not eir inspiration to their normal resting respira hence their tidal volume during the exercises art or all of their normal tidal volume above

iration of exercise breathing was nearly as he patient could achieve in attempting to is vital capacity This depth was obtained exercises as it had been in the vital capacity considerable lengthening of the time taken to breath the average respiratory rate being eaths a minute Inspiration was rapid consumption was not altered to any significant en measured over a three minute period of exercises in each patient This was shown by nged resting respiratory level when natural was resumed after the period of exercise

e increased tidal volume of exercise-type helium was mixed more rapidly in the lungs natural breathing The mixing curve in which

TABLE III—MEAN RESULTS OF VENTILATORY FUNCTION TESTS DURING NATURAL BREATHING AND EXERCISE TYPE BREATHING

| — | Breathing | Mean | S D |
|---|---|---|---|
| Tidal volume | N | 0 54 | 0 12 |
| | E | 0·92 | 0 19 |
| Respiratory rate | N | 19 5 | 4 46 |
| | E | 9 0 | 1 77 |
| Minute volume | N | 10·04 | 1 43 |
| | E | 8 15 | 2·04 |
| Effective tidal volume | N | 0·09 | 0·03 |
| | E | 0 31 | 0 10 |
| Effective minute volume | N | 1·69 | 0 14 |
| | E | [illegible] 70 | 0·93 |
| E T V T V (%) | N | 16 8 | 3 49 |
| | E | 32 0 | 6 19 |
| Mixing efficiency (%) | N | 51·0 | 12 37 |
| | E | 48 6 | 9 43 |
| Poorly ventilated space/functional residual capacity (%) | N | 24 3 | 4 47 |
| | E | 25 5 | 6 69 |

E exercise type N natural
All volumes corrected to 37°C and recorded to nearest 0 01 litre

the decrease of concentration of helium in the spirometer circuit is plotted against time was consequently much steeper It still showed however an inflection at the same point on the ordinate scale as was found in the mixing plot with natural breathing The poorly ventilated space was thus unaltered in size Furthermore although the two component lines of the mixing plot were both steeper than those obtained with natural breathing mixing of helium their slope relative to each other remained the same The mixing efficiency was consequently unchanged by exercise type breathing

During natural breathing in all patients an abnormally small fraction of each breath was effective in mixing the inspired helium in the lungs. Exercise type breathing produced an increased effective tidal volume and the effective tidal volume/tidal volume ratio was also increased This led to an increase in the effective minute volume in every patient despite the reduced total minute volume in 10 of them

*Electromyography*

When the patients did not consciously breathe as they had been taught there was no change in the electromyographic pattern either during quiet breathing or when the ventilation was increased by rebreathing expired air Recordings made when the patients performed their exercises showed activity in the abdominal muscles This was always considerably greater in the oblique

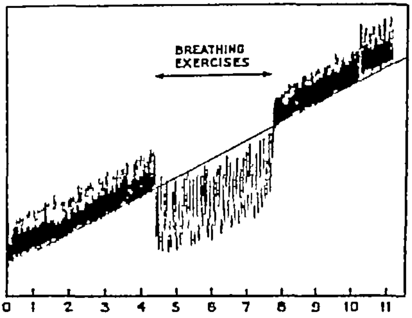

Fig 2—Case 5 : record of respiration and oxygen consumption in two periods of natural breathing with a period of breathing exercises between them. Read from left to right. Inspiration upwards.

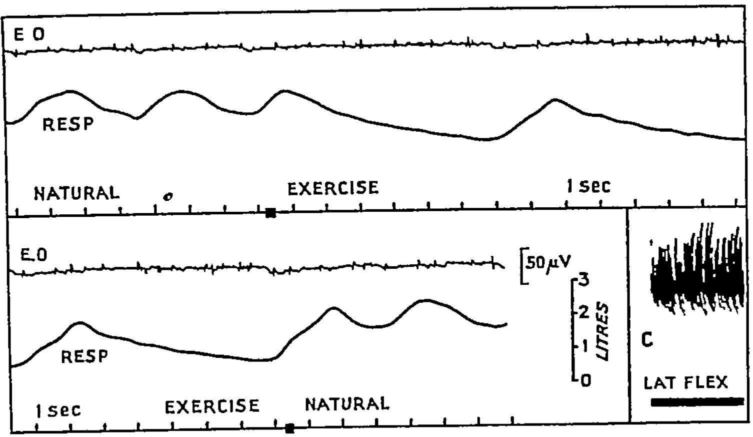

Fig 3—Case 13 E O electromyogram from external oblique muscle , Resp, respiration (inspiration upwards)

A and B, continuous record beginning and ending with natural breathing between signal marks is a period of breathing exercises in which there is only slight activity in the external oblique (no activity was detected in the rectus abdominis)

C, record taken when patient tried to bend sideways no actual movement took place but activity recorded was considerable

muscles than in the rectus abdominis The muscular activity developed during the exercises was slight compared with that produced on voluntary expiratory efforts (fig 3), except in the 2 patients who had shown expiratory activity in the abdominal muscles before being treated with the exercises

A reduction in the intensity of the activity in the sternomastoid muscle during exercise type breathing was observed only occasionally The explanation for the continued inspiratory action of this muscle appeared to be that, although inspiration took place below the normal resting respiratory level, the rate of inspiration during the exercises was increased

During rebreathing from the spirometer the patients had to be exhorted continuously to " breathe as you were taught," for they tended to stop doing their exercises (shown by a reduction of intensity of their expiratory abdominal contractions) as their ventilation increased (fig 4) When the patients were recovering from this hyperventilation, their abdominal contractions stopped despite obvious and considerable breathlessness

## EFFECTS OF BREATHING EXERCISES

In a follow-up of about three months, during which the patients continued to practise their exercises, it was found that, when they breathed naturally, the exercises had not significantly altered the total capacity of the lungs, the relative sizes of their component parts, the method of mixing inspired air in the maximum breathing capacity

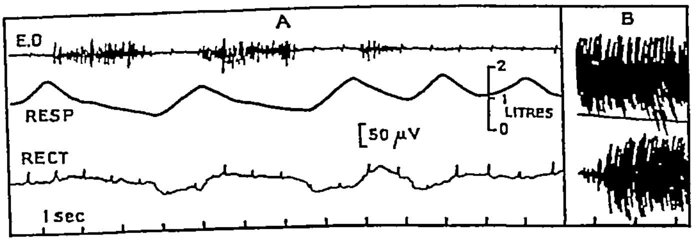

Fig 4—Case 8 : E.O., electromyogram from external oblique muscle Rect., that from rectus abdominis , Resp, respiration (inspiration upwards)

A, end of a record taken while patient was rebreathing expired air to the limit of tolerance although the external oblique contracted initially to a moderate extent, the contractions ceased as the patient distressed

owards end of voluntary maximal expiration, showing large of activity of which the muscles are capable

### Discussion

All our patients had been edly, and their ventilatory been tested on numerous oc they were taught breathing This long period was erately so that the bre should be started only when were no longer improving and the results of tests of function showed no trend of When the exercises were summer, we thought that th had been reduced as much as that any learning factor af had been overcome The variation of the ventilatory f was then no greater than repetition of the tests on the (Friend 1954)

We did not intend a long tion of the effects of bre and so did not attempt to observations by the provision patients For an investigation of the " im of the exercises no such control was necessar

The " immediate action " of breathing exe patients was as follows (1) there were the rate and an increase in the depth of (2) despite the slower rate of breathing the the effective tidal volume was so great that minute volume was larger than in natural (3) the " mixing efficiency " and " poo space " were unaltered , (4) there was a respiratory level, with the result that the c inflated during the exercises , (5) expirato prolonged , (6) there was no change in the activity of the sternomastoid muscle, but muscles, which were usually inactive breathing, were used when the exercises wer The intensity of this activity was gre oblique muscles than in the rectus ab slight compared with the potential acti muscles

The theoretical aims of breathing exer examined in the light of our findings

(1) *To relax the accessory muscles of inspira* of our patients there was complete and rapid the sternomastoid muscle at the end of insp breathing exercises were taught Relaxation ated by the exercises There is no reason to further " active " relaxation might be obtained

(2) *To increase diaphragmatic movement by of the costal margins by contraction abdominal muscles*—Wade (1954) has the diaphragm cannot be controlled has directed attention to the falla conclusions about the extent of movement from movements of the ante wall We were impressed by the patients paid to trying to move par and abdominal wall selectively evidence that these efforts affected ve tion They did, however, add greatly difficulty in learning the exercises

(3) *To obtain use of the lung bas lateral basal expansion*—There is no sume that selective movement of a of chest wall is necessarily accompa ventilation of the underlying lung ventilatory function showed no redu of the " poorly ventilated space " ment in the " mixing efficiency " wh performed breathing exercises

*make expiration the active phase of respiration* —This wo separate actions (*a*) prolongation of expiration crease of the depth of expiration Merely prolonging ion of expiration has no value As expiration is in emphysematous patients the rate of expulsion reases greatly Exercise type breathing demands omplete expiration for each breath and produces a ratory rate of about 9 a minute This causes a of the minute volume at a level below that needed noderate physical exertion. Our patients could not heir exercises during physical activity and had then to natural breathing

as ventilatory function is concerned the changes have found with breathing exercises are those eep breathing

immediate action of the exercises on the s of breathing may warrant further attention on is mechanically inefficient in ventilating the emphysema where the chest is raised and l and the diaphragms are flattened and depressed ver the chest is deflated by a preliminary n, the inspiratory muscles can act more effici urthermore, initial deflation of the lungs and wering of the end expiratory level increase the mixing of inspired air in the lungs as Bates 954) demonstrated in healthy people by the clearance method

expiration would be achieved as effectively by expiratory exercises used by Reed (1952) to breathlessness, without the disadvantages to the prolongation of expiration of the long n exercises A simple sharp contraction of all ominal muscles would produce as great an of the diaphragm as do the complicated to lower the costal margins by contraction of l abdominal muscles alone in the long-expiration

gh our patients did not make full use of active n when they did their exercises several of them eathless by physical exertion appeared to be of their dyspnœa more rapidly by exercise than by natural breathing This is the only that we have obtained of any benefit to be d to the exercises, but it was not controlled by on or blood gas studies

was no question of strengthening the abdominal y the exercises, for they were adequately devel all patients and, judged electromyographically reserves (figs 3 and 4)

not easy to foresee any ' effect of breathing even if practised for a long time It is difficult ne that breathing could ever be so radically that expiration should become the active phase ents showed no signs that their usual mode of had been altered in any way by the exercises. l performed them as a set and conscious act

## Summary

immediate action of breathing exercises has died in 12 emphysematous men by tests of ry function and by electromyography

hanges found were those associated with slow athing in an increasedly expiratory position

hort period of time the exercises produced no upon ventilatory function

h to thank Prof A. Kekwick and Prof Samson n whose departments this work was done for their advice; Mr W F Floyd for his guidance with the ography; Mr E. E Dowset for his technical Dr K W Donald and Dr F H Scadding for he manuscript; Miss M C Devers and Miss R for teaching the exercises to our patients and the or their ready coöperation The electromyographic ported here formed part of a thesis by one of us ) accepted for the doctorate of philosophy by the of London This work was done during the tenure of the Saltwell scholarship of the Royal College of Physicians by one of us (J F)

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# TETANY COMPLICATING THE TREATMENT OF POTASSIUM DEFICIENCY IN RENAL ACIDOSIS

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TETANY has been described in patients with potassium deficiency and has been reproduced experimentally during potassium deficiency in normal persons (Fourman 1954) Potassium deficiency due to an abnormality of renal function has also been described before usually but not always associated with a renal acidosis and often also with a concomitant loss of calcium or phosphate (Brown et al 1944 Albright et al 1946 Hadorn 1948 Earle et al 1951, Milne et al 1952 Squires et al 1953) These specific renal lesions have not yet been produced experimentally and the potassium deficiencies associated with them can be studied only by the observations and tests which it is possible to make on patients

Our reasons for describing this case are (1) to show how tetany as a complication of recovery from potassium deficiency dominated the whole treatment of the patient (2) to place some of the results on record for future reference and (3) to make some comments of a more theoretical nature on the causation of the tetany

## Methods

Sodium and potassium were determined with an internal standard flame photometer The pH was determined with a glass electrode at 37°C and the measurements were checked by the determinations of plasma bicarbonate and alveolar carbon dioxide The analysis of muscle was based upon Mudge and Vislocky (1949) Other methods were based upon Hawk et al. (1947)

## Case report

A.B was a single woman born in 1909 Her health had been good until November 1951 when she noticed that she easily became breathless; she began to have nocturia and was abnormally thirsty She had never had dysuria hæmaturia, or œdema.

In February 1952 she had an emergency laparotomy in Norwich for an attack of lumbar and abdominal pain, and a normal appendix was removed After the operation she collapsed and remained in stupor for a week with a flaccid paralysis of her face neck and limbs accompanied by difficulty in swallowing weakness of the voice and very severe constipation when conscious she had double vision. She was given some potassium chloride and she recovered from her paralysis but the treatment was then abandoned She continued to have three or four attacks of paralysis a month, each lasting for a few days. No potassium was given for these attacks. She remained very ill, and vomited nearly every morning; in 6 months she lost 70 lb in weight

In July 1952 she was admitted to the East Suffolk Hospital under Dr Ronald Jones. Her alarming condition first led to the diagnosis of an addisonian crisis , but her serum potassium was found to be only 1 8 m eq per litre, and potassium chloride was immediately administered She rapidly became stronger, and after taking 200 m eq (15 g ) daily for a fortnight she could walk for the first time in 5 months and was no longer constipated A smaller dose failed to control her symptoms, and treatment with 200 m eq of potassium chloride was therefore continued At this time she began to gain weight

In August, 1952, she began to have attacks of tetany once or twice a week, lasting from 15 minutes to several hours She had a feeling of coldness and tingling in her limbs before the attacks, and then her hands, her feet, and her face went into spasm and her limbs were covered with sweat The spasms might begin at any time of the day, and, although they were apt to come on soon after a dose of potassium, they occasionally started early in the morning before she had had any treatment for that day Calcium, given as 6 g of the gluconate daily by mouth, did not prevent the attacks, and we subsequently established that injections of calcium gluconate, up to 4 g intravenously, did not shorten them There was never any suggestion of overbreathing or air hunger, and the attacks were not relieved by breathing into a bag or by breathing 5% carbon dioxide Measures calculated to reduce the serum potassium, such as the administration of glucose or the injection of adrenaline (Castleden 1938), have since been found to have no effect

At the time of the attacks of tetany A.B sometimes had œdema of the eyelids and of the ankles, which had been preceded by excessive thirst Trousseau's sign could often be elicited, but her spasm relaxed slowly when pressure on the nerve trunk was released , consequently we were unable to reproduce Lewis's observations (1942) on the phenomenon In her, therefore, the spasm may have been due to more than ischæmia of the nerve trunk

## ROUTINE INVESTIGATIONS

When the patient was admitted to Addenbrooke's Hospital in July, 1953, for further investigation, no potassium chloride had been administered for 3 weeks except on four occasions to relieve attacks of transient paralysis

On admission she was found to have only 2 5 m eq of potassium per litre of serum At the same time she had 116 m.eq of chloride and 18 7 m eq of bicarbonate The serum calcium was 9 1 mg per 100 ml The rest of her serum electrolytes (sodium, phosphorus, and magnesium) were normal, but in spite of the acidosis her urinary pH was of the order of 7 0 The urine usually contained a trace of protein and a heavy deposit of phosphates , it contained no sugar, very little ammonia, and no abnormal cells or casts, and it was always sterile The specific gravity was 1010 after depriving the patient of water for 18 hours The blood urea, which had been 25 mg per 100 ml in July, 1952, was now 38 mg , and her urea clearance was 49% of normal Her endogenous creatinine clearance was 53 ml per min , and she excreted only 50% of 6 mg of phenosulphonephthalein in 2 hours and 40% of 1 litre of water in $2^1/_2$ hours Her glomerular and tubular function, therefore, were both well below the normal X ray examination revealed renal calcinosis

She excreted large amounts of potassium even when the serum potassium was low, and occasionally, as in similar cases (Earle et al 1951), her renal clearance of potassium was greater than could be accounted for by glomerular filtration Her kidneys conserved sodium well when the intake of sodium was very small and she maintained a normal calcium balance Her clearance of phosphate averaged 11 2 ml per min over 24-hour periods and was within normal limits although her glomerular filtration rate was low (Milne et al 1952)

The only other abnormal finding was the high concentration of the proteins in the plasma , fractionation and paper strip electrophoresis showed that the increase was entirely in gamma globulin Her liver was, however, functionally normal and she had no evidence of sarcoidosis

## SPECIAL INVESTIGATIONS AND TREATMENT

Many minor investigations, balance experiments, and a muscle biopsy have been made on this patient, and only a summary of the pertinent ones will be given here

### *Characterisation of the Renal Acidosis*

112 m eq of ammonium chloride was given daily for 3 days when the patient had been receiving 200 m eq of potassium daily for some time as the chloride, and no citrate was being given. The serum bicarbonate fell from 14 3 m eq to 10 7 m.eq per litre and the chloride, which was alre m eq , scarcely changed There was little cha of her urine or of her plasma, which at this ti The urinary ammonium and titratable acidity slightly The sodium excretion rose by 71 m.e the potassium by 60 m eq and the calcium by

### *Effects of Treatment with Potassium Chloride*

When she was first admitted to Addenbrooke and was not having any treatment, she was losing about 44 m.eq of potassium daily and potassium was 2 5–3 0 m eq per litre Under tre 200 m eq daily she retained 600 m.eq in 3 week time her serum potassium was normal , but she acidosis similar in magnitude to the one she admission and her plasma pH ranged between 7 She had only occasional cramps at this time.

### *Effect of Treatment with Citrate*

Some time after she began to have periodic tetany in Ipswich, Dr Jones changed her tre 200 m eq of potassium chloride daily to 140 m.eq. of citrate This made her tetany so much worse that gave up the citrate and returned to the chloride had been re established at Cambridge on potass alone, the advantages which would probably be acidosis could be corrected made us give her 1 sodium citrate daily, and we were then able to redu of potassium chloride from 200 to 50 m.eq d treatment made her serum chemistry entirely raised the plasma pH to 7 4, but the patient the mittent attacks of tetany At this time the was 9 6 and the plasma bicarbonate 26 m.eq p spite of her tetany she began to put on weight and than she had done for a couple of years O potassium chloride completely for a week did not tetany

On 50 m eq of potassium chloride daily plus sodium citrate she still had some attacks of teta her serum bicarbonate was only 17 m eq per litre. the administration of potassium and also a hig sodium citrate appeared to aggravate her tetany, of potassium was kept as low as possible, and all of as the citrate, and the sodium citrate correspon Thus, 30 m eq of potassium citrate plus 75 m.eq. citrate kept her serum bicarbonate normal and did any serious attacks of tetany for several months, she had gained 20 lb in weight (from the time of to Addenbrooke's) and was scarcely recognizabl who had not seen her since then After about 5 had some quite severe attacks of tetany with œdem her serum potassium had fallen from 4 to 3 3 m and this suggested that she might be better with sium but less sodium citrate Consequently her has now been changed to 60 m eq of potassium of sodium citrate, and this controls her acidos potassium deficiency, but she still gets occasional tetany in her hands and feet

### *The Muscle Biopsy*

On Feb 10, 1954, at 4 P M , under a general a portion of the patient's triceps was removed She attack of tetany that day at 9 A.M The serum c the time of operation and the composition of muscle are shown in the accompanying table obtained may be compared with those of Talso et who analysed portions of normal skeletal muscle sixteen adult men and women All the values fall limits found by Talso et al , but the concentration and potassium were both in the upper ranges of the sum of the two exceeded the average of Tal more than twice the standard deviation

SERUM AND MUSCLE CHEMISTRY AT 4 P M ON FEB
THE PATIENT HAD HAD AN ATTACK OF TETANY

| — | Serum |
|---|---|
| Protein nitrogen × 6 25 (g per 100 g ) | 8 6 |
| Fat | |
| Water (by evaporation) | |
| Sodium (m eq per litre of water) | 155 |
| Potassium (m eq per litre of water) | 4 2 |
| Chloride (m.eq per litre of water) | 116 |

* Calculated as in Lowry and Hastings (194

## Discussion

*of Treatment*

atients with an acidosis excrete large amounts
a in their urine and may in consequence get
of their kidneys. This patient's kidneys were
although she was excreting very little calcium
ne, and alkalinity of the urine was probably th
t was established both at Ipswich and at
e that the administration of calcium salts did
e her tetany This was a valuable discovery
itural temptation might have been to treat her
um and the result could only have been further
of calcium salts in and around her tubules
not due to a calcium deficiency is usually
l with an alkalosis of the extracellular fluid and
y of potassium deficiency has been attributed
y Darrow et al. (1948) Our patient's tetany
was not controlled by breathing 5% carbon
r by rebreathing her own expired air which
m to suggest that the cause was not simply an
ular alkalosis. *Nevertheless, once her potassium*
y had been corrected, her tetany seemed to
vated by the subsequent correction of her
ular acidosis

*lem of the Tetany*

and Milne (1952) induced potassium deficiency
intake of sodium was generous They found
potassium deficiency was associated with an
ular alkalosis and probably less Na + K than
the cells. They *did not produce tetany at any*
their experiments Fourman (1954) induced
n deficiency while the absorption of sodium was
ry small The deficiency of potassium was
*nied by an acidosis of the extracellular fluid and*
less than the normal amount of Na + K in the
he administration of sodium at this stage in
mparable to those of Black and Milne, corrected
acellular acidosis without inducing an obvious
and the subjects got tetany Balance experi
ndicated that the sum of the Na + K ions in
was high at this time The tetany in these
nts was preceded by the appearance of œdema
y was repeatedly observed in our patient (*a*) when
as no hypocalcæmia (*b*) when there was no
in the extracellular fluids and (*c*) when no
crease in the serum potassium had taken place
lford 1954) Thus none of the well known
sms can be invoked to explain it. It was first
l by the administration of *potassium chloride,*
presence of a normal serum potassium and a
ced extracellular acidosis and it has frequently
served since with a normal serum chemistry
ere was no change in the extracellular fluids to
for our patient's tetany—and this may also be
persons suffering from overbreathing tetany
o 1932)—a change in the composition of the
ular fluids may be more important in the pro-
of tetany than the changes in the extracellular
ich are generally regarded as responsible
nce that the intracellular fluids are alkaline in
nics of potassium deficiency or at any rate con
re than the normal concentration of Na + K
present on our patient's biopsy and Fourman's
alance studies Furthermore there is no evidence
ges in the composition of nerves and information
oth these points is desirable
over the mechanism of this patient's tetany
ersonal idiosyncrasy must be invoked to explain
remained so prone to tetany for such a long time
r potassium deficiency had been made good and
um chemistry had been satisfactorily corrected
is not the reaction of a normal person although
athing tetany *is occasionally induced remarkably*
It may be that our patient's cells are peculiarly sensitive to external changes such as the correction of an extracellular acidosis which would by themselves be insufficient to induce tetany in an experimental volunteer; but it seems more probable that her cells are themselves abnormal in the way in which they take up and retain potassium and perhaps sodium as well.

## Summary

A patient with potassium deficiency due to renal acidosis developed severe tetany when her *serum* potassium was raised to normal by the administration of potassium chloride

Her serum chemistry during the attacks was normal except for the acidosis which was not corrected by the potassium chloride

Her tetany was not relieved by the administration *of calcium or by breathing 5% carbon dioxide*

The most successful method of correcting the potassium deficiency and the acidosis while avoiding tetany as far as possible has been to give relatively small doses of potassium and sodium citrates.

No facts known at present will explain this patient's tetany and it has been suggested that it is due to a derangement of the normal control of the intracellular pH or cation concentration

*We are indebted to Dr Ronald Jones for bringing the* patient to our notice to Dr A. B Morrison, Dr G R Hervey and Dr J R Robinson for help at all stages of the investigation to Dr R N Laurie and members of the department of clinical biochemistry, Addenbrooke's Hospital for a large number of routine biochemical investigations; to Mr R W Butler F.R.C.S for performing the muscle biopsy and to Mr J Dickerson B.SC and Miss E Colbourn and Miss Anne Stockbridge for their assistance

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# MALIGNANT ARGENTAFFINOMA

## WITH CYANOSIS AND PULMONARY STENOSIS

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The association of malignant argentaffinoma with cyanosis and pulmonary stenosis was first recognised by Björck et al (1952) An account of Björck's original case and of five others was given recently by Thorson et al (1954) who discussed ten further cases that had been published elsewhere including three with similar features reported by Isler and Hedinger (1953) Branwood and Bain (1954) have lately discussed in these columns a case which they recognised in retrospect as having the syndrome first described by the Swedish workers We now present two further examples of this interesting condition

**Case 1**—A housewife, aged 63, was admitted to hospital in November, 1952, complaining of intermittent attacks, over eighteen months, of watery diarrhœa and lassitude In October, 1951, she had noticed a patchy bluish coloration of the skin which became increasingly obvious during the next year Four months before admission œdema of the legs developed.

*On admission* the most striking feature was the appearance of the skin, which was brick red in colour, with blotchy areas of cyanosis, the discoloration, which varied from time to time, was most prominent on the trunk (fig 1) Blanching could be produced by pressure There was pitting œdema of the legs The jugular venous pressure was not raised A loud systolic murmur was heard over the whole precordium The pulse rate was 76 per min and regular The blood pressure was 95/65 mm Hg The liver was palpable 6 cm below the costal margin, and had a firm irregular surface

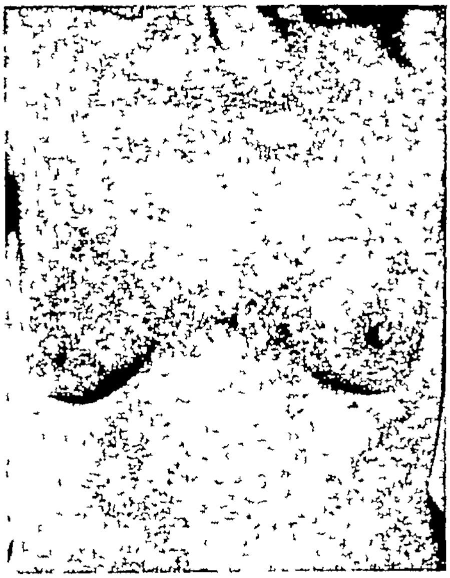
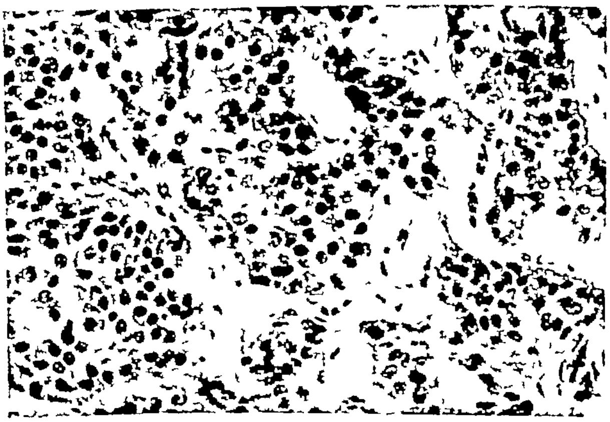


Fig 1—The skin appearance in case 1

*Investigations*—Hæmoglobin 72% (10 7 g per 100 ml), red cells 4 3 million per c.mm, white cells 10,000 per c.mm, with a normal differential count Erythrocyte sedimentation rate (E S R) 5 mm in one hr (Westergren), bleeding time (Duke) two min. Spectroscopy revealed no abnormal blood pigments Radiography of the chest showed that the transverse diameter of the heart was normal An electrocardiogram revealed myocardial damage Radiological examination of the gastro intestinal tract showed that in the region of the distal jejunum and proximal ileum there was segmentation which altered during the examination and could be obliterated by palpation, indicating that it was due to variations in muscle tone A biopsy of skin showed intimal thickening and narrowing of the small arterioles

*Progress*—The diarrhœa and œdema persisted She was mentally alert until two weeks before her death when there was an abrupt change in her personality, she became confused, and the cyanosis became much deeper She died in coma, ten weeks after admission

*Necropsy* (Dr R Cureton)—The colour of the skin after death was much less striking than during life The heart weighed 260 g and showed no obvious abnormality of the valves or cavities In the medial wall of the cæcum there was a whitish growth measuring 3 5 × 3 0 adjacent lymph nodes were infiltrated by simila rest of the large intestine and the small normal The liver weighed 1940 g and of white metastases, up to 2 5 cm in diamete contained white rounded masses All other normal, apart from the lungs, which bronchopneumonia


I : the primary growth in the cæcum ( ×230)

*Histological examination* of the cæcum growth was in the submucosa, infiltrating the extending at one point into the mucous arrangement and shape of the cells were those of noma (fig 2) and this was confirmed by staining granules in the cytoplasm of the cells with similar characteristics were present in lymph nodes, the liver, and the ovaries

**Case 2**—A housewife, aged 59, was admitted in May, 1953, complaining of shortness of mittent diarrhœa of two years' duration Four admission she noticed swelling of the abdomen, weeks there had been swelling of the ankles. previous history of rheumatic fever

*On admission* a malar flush was present The were engorged up to the angle of the jaw and The heart did not appear to be enlarged clinically, systolic murmur was audible at the apex, the and, loudest of all, at the pulmonary area The pulse was regular at 68 per min, and the blood pressure was 90/68 mm Hg The abdomen was distended with ascites, after paracentesis, which yielded clear straw-coloured fluid, the liver was found to be hard and to extend 5 cm. below the costal margin Œdema of the legs extended up to the

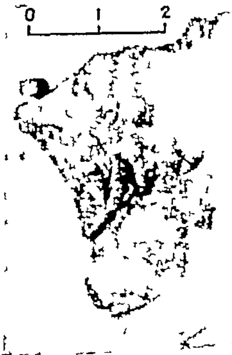


Fig 3—Case 2: specimen showing growth (outlined) in the

*Investigations*—Hb 98% (14 5 g per 100 ml), 5 4 million per c mm, white cells 4000 per normal differential count E S.R 4 mm in one ho gren), serum proteins 5 7 g per 100 ml. (alb globulin 1 3 g), electrophoretic pattern bromsulphthalein test suggested severe liver Chest radiography and fluoroscopy revealed a sided pleural effusion and elevation of the right diaphragm There was slight enlargement of ventricle, the pulmonary artery shadow was and the peripheral pulmonary vessels were poorly left auricle was not enlarged An electrocard inversion of T waves, due to digitalis therapy, PQRS waves

*Progress*—On these findings a diagnosis of stenosis and congestive heart failure was made was treated with digitalis and mersalyl. The tinued and she became more cachectic She d eight weeks after admission

*Necropsy*—The body was grossly wasted. The cavity contained about four pints of serous fluid half way along the ileum there was a hard white nodule measuring 1 0 × 1 0 × 0 25 cm (fig 3) of the intestine was normal Two enlarged were seen in the porta hepatis The liver we and in the right lobe there was a hard white ma diameter (fig 4) The heart weighed 315 g The appeared normal, all valve cusps showed some but the chordæ tendineæ and papillary muscles There was stenosis of the pulmonary valve, the one finger tip only The tricuspid orifice was dilated The aortic and mitral orifices were All other organs were normal, apart from the showed areas of bronchopneumonia

*Histological examination* of the nodule in the invasion of the submucous and muscle coats by

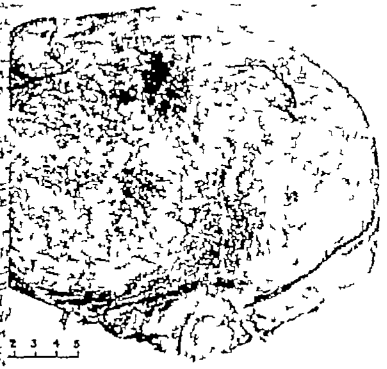


Fig. 4—Case 2: metastases in the liver

c growth which was also infiltrating the lymph The cells of this growth were spheroidal and had taining rounded nuclei; they were arranged in masses ndency to gland formation The appearances were an argentaffinoma (fig 5) Sections of the liver and ymph nodes in the porta hepatis showed similar tissue

## Discussion

series reported by Thorson et al (1954) the ndings were malignant argentaffinoma of the with metastases in the liver a peculiar patchy and transient vasodilatation of the skin ry stenosis, and tricuspid incompetence Diar d peripheral œdema were commonly present and instances there was ascites

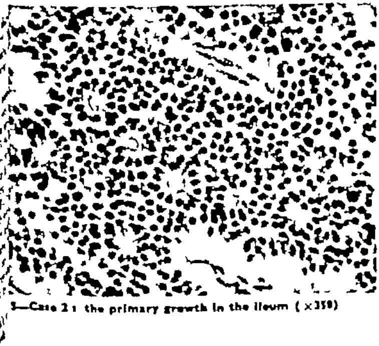
wo cases reported here both presented with long diarrhœa and peripheral œdema with the of ascites in case 2 The vasomotor changes the skin in case 1 are so characteristic that et al. maintain that their recognition should presumptive clinical diagnosis of metastasising finoma Although valve lesions were not found at necropsy a loud precordial systolic murmur rd during life Case 2 did not show widespread but only a malar flush In this case however as clinical evidence (confirmed at necropsy) of ary stenosis and tricuspid incompetence In both ropsy revealed an argentaffinoma of the intestine had metastasised extensively—to the liver odes, and (in case 1) ovaries.

ms that widespread metastases are necessary and cardiac lesions to develop since these have not been reported in cases in which the argentaffin tumour remained localised to the intestine

The importance of this syndrome lies in the fact that, according to Thorson et al, it probably results from an excessive secretion of 5 hydroxytryptamine This substance, also called enteramine has been found in normal intestinal mucosa (Dalgliesh et al 1953) It is present in normal serum and blood platelets and, because of its vasoconstrictor properties has been called serotonin (Rapport 1949) Lembeck (1953) showed that extracts of a benign argentaffinoma contained hydroxytryptamine, and recently Pernow and Waldenström (1954) have demonstrated very large amounts of this substance in the serum of two patients suffering from metastasising argentaffinoma with vasomotor skin changes

The action of hydroxytryptamine in man has not yet been completely elucidated It certainly causes contraction of the smooth muscle of the intestine, and in case 1 the diarrhœa was associated with radiological evidence of excessive peristalsis remote from the site of the tumour Reid and Rand (1952) have shown that hydroxytryptamine injected intradermally causes local congestion and venous spasm and probably this would explain the skin colour in case 1 Woolley and Shaw (1954) believe that hydroxytryptamine has important effects on the central nervous system and that certain psychoses such as schizophrenia may be related to an abnormal concentration of this substance case 1 undoubtedly showed mental changes of a confusional type during the last two weeks of her life

The cause of the cardiac valve lesions remains obscure In case 2 the pulmonary vessels were not easily seen during fluoroscopy possibly hydroxytryptamine causes constriction of these vessels which if continued long enough results in permanent stenosis.



5—Case 2: the primary growth in the ileum (×350)

## Summary

Two cases of malignant argentaffinoma of the intestine with metastases in the liver are reported One was associated with a peculiar patchy cyanosis, and the other showed pulmonary stenosis and tricuspid incompetence.

The view that this syndrome results from an excessive secretion of 5 hydroxytryptamine by the tumour is discussed

We wish to thank Dr A. W Spence and Dr R Bodley Scott for permission to publish these cases and Prof J W S Blacklock for his help and advice We are indebted to Dr R Cureton for the necropsy report of case 1

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It may be that the next development of communications theory will be in the heart of the cell where information seems to flow steadily from the genes to the functional and productive divisions of the cell through chains of patterned macromolecules no doubt the inevitable feedback controls are similarly mediated In many ways the most effective way of picturing the activity of the influenza viruses and perhaps of many other viruses is to think of them as a set of punch-cards maliciously inserted into vital parts of a fantastically complicated computing machine An essential part of the machine's activity is to produce also in the form of punch-cards new programmes for its own functioning Something analogous to virus action would result when the machine found itself compelled to produce programmes that would lead inevitably to its malfunction or destruction. —Sir MACFARLANE BURNET F.R.C.P. F.R.S. *Endeavour* 1955 14 5

# SPONTANEOUS HYPOGLYCÆMIA DUE TO ISLET-CELL TUMOUR OF THE PANCREAS

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Localised islet cell tumours of the pancreas are grouped by Whipple (1944) into four groups (1) typically adenomatous, (2) less well differentiated, with cells in ribbons, or scattered collections with degenerated fibrous tissue, (3) poorly differentiated, with possible malignancy and invasion of the capsule, and (4) definitely malignant, with lymph node and other metastases

They are usually found in the body or tail of the pancreas, often deep seated, and are described as reddish-purple in colour They are generally amenable to operation, but occasionally numerous adenomata of the islet cells are found diffusely scattered throughout the pancreas, and in these cases surgical removal is impracticable

## Case-report

A man, aged 58, first attended hospital as an outpatient on Oct 3, 1953, complaining of pain in the right wrist, which subsequently proved to be the site of early rheumatoid arthritis On entering the consulting room in the outpatient clinic he staggered about as though drunk and was sweating slightly His wife, who was with him, said that for about two years he had had frequent episodes of this nature, which had recently been investigated elsewhere and diagnosed as hypertensive encephalopathy The possibility of hypoglycæmia was considered, and his blood sugar level was immediately determined as 23 mg per 100 ml Oral glucose was administered, two hours later his blood sugar level was 30 mg per 100 ml, and he was still behaving as though drunk He was then given intravenous glucose, and at once his behaviour became normal. He was admitted for investigation the same day, with a tentative diagnosis of islet-cell tumour of the pancreas Questioning revealed that the attacks usually occurred two or three hours after a meal or after exercise The patient became confused and did not know what he was doing, he made the spontaneous remark that he always recovered after a meal or if he was given a cup of sweet tea

*Treatment*—He was given a diet liberal in carbohydrate and had no attacks as long as this was continued

*Laboratory Investigations*—A glucose tolerance test (three days after admission) gave the following blood sugar levels fasting 15 mg per 100 ml, $^1/_2$ hr after 50 g of glucose 85 mg per 100 ml, 1 hr after glucose 77 mg per 100 ml, $1^1/_2$ hr after glucose 58 mg per 100 ml, 2 hr after glucose 38 mg per 100 ml, and $2^1/_2$ hr after glucose 25 mg per 100 ml Neither glycosuria nor ketonuria was found The blood urea level was 42 mg per 100 ml Liver function tests gave the following results serum alkaline phosphatase 13 King Armstrong units, serum proteins 7 6 g per 100 ml (albumin 4 2 g per 100 ml, globulin 3 4 g per 100 ml, albumin/globulin ratio 1 2 1), thymol turbidity 1 unit, thymol flocculation negative, prothrombin time 10 sec, and urinary excretion of 17 ketosteroids 7 9 mg in 24 hr

*Laparotomy* was done by Mr R Petticrew on Nov 10, 1953 A hard nodule was felt at the junction of the body and the tail of the pancreas, and this proved to be a well encapsulated whitish tumour, which it was thought might possibly be malignant because of its colour and consistence For this reason partial pancreatectomy was done, together with splenectomy, and the tumour was sent for histological examination Dr J E Ennis reported as follows "Specimen consists of the tail and body of pancreas, 6 cm. long In the middle of this tissue is a firm white well defined oval tumour 15 × 11 × 9 mm. Histological examination shows a scirrhous tumour in which there are groups of pancreatic cells, some with acinar arrangement The nuclei of these cells are somewhat irregular, but mitotic figures are scanty, and there is no obvious invasion of blood vessels There is no definite capsule present Presumably a benign pancreatic islet cell adenoma" Sections of the tumour were also referred to a consultant panel in morbid histology, who agreed that the tumour was benign

*Postoperative Progress*—Two hours after blood sugar level was 330 mg per 100 ml., and i between 200 mg and 650 mg per 100 ml. for th day, requiring control with insulin A week after t the fasting blood sugar level was 175 mg per 10 then settled down to about normal A gluc test on Dec 3, 1953, gave the following blood- fasting 100 mg per 100 ml, $^1/_2$ hr after 50 g 175 mg per 100 ml, 1 hr after glucose 175 mg 1 $1^1/_2$ hr after glucose 150 mg per 100 ml, and 2 hr a 150 mg per 100 ml This suggested a low r insulin because the blood sugar level did not retu after two hours Neither glycosuria nor ketonur

*Follow up*—The patient was seen as an outpatie 1954, when he was feeling well, and again on Fe glucose tolerance test gave the following blood- fasting 120 mg per 100 ml, $^1/_2$ hr after 50 g 190 mg per 100 ml, 1 hr after glucose 190 mg p $1^1/_2$ hr after glucose 200 mg per 100 ml., 2 hr a 130 mg per 100 ml, and $2^1/_2$ hr after glucose 1 100 ml—i e, a curve just higher than normal minor insulin deficiency Neither glycosuria n was found In February he returned to work a face, after being unemployed for more than two y on Aug 13 he was very fit and working regularly been no hypoglycæmic attacks since before h and a glucose tolerance test gave the following b levels fasting 90 mg per 100 ml, $^1/_2$ hr after 50 g 178 mg per 100 ml, $1^1/_2$ hr after glucose 115 mg and 2 hr after glucose 85 mg per 100 ml

## Comment

The interesting feature in this case was th appearance of the tumour These adeno invariably been described in published reports a purple, this one was white, leading to a p diagnosis of malignant adenoma and the remov pancreas than would otherwise have been rem the result that the patient became severely hyp after the operation

Our thanks are due to Mr R Petticrew, F.R.C operation, and to Dr J E Ennis for the histolo

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# Preliminary Communication

## EXCRETION OF ETHANOLAMI PHOSPHORIC ACID IN CŒLIAC D

In the past three years we have examined partition chromatography the urine of 53 chi cœliac disease We report here an observat we believe has not so far been recorded

In 30 of these children a substance was d the urine which corresponded to the positio for ethanolamine-phosphoric acid [1] No spot for ethanolamine, nor was any other constant a noted in the urine The diagnosis of cœli was established by the characteristic history a appearance and was supported by the customa gations The substance was detected in the uri as 3 months and as late as 12 years of ag present intermittently regardless of diet, other treatment, or the stage of the disease

The demonstration of an amino acid in th of ethanolamine phosphoric acid in the urine o with symptoms suggestive of cœliac disease m help in diagnosing the disorder Should thi prove to be ethanolamine phosphoric acid, fu may be shed on the mechanism of the disease, amine phosphoric acid has been recovered from intestine of rabbits and pigs [2] so three years a total of 700 urinary amino acid -ograms from 600 patients have been completed ie patients were adults (124 men 101 women) e children below 13 years of age (164 boys 75 sex not recorded) and 102 of the childre than 1 year of age

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[1] Dent C E *Biochem J* 1948, 43, 169
[2] Colowick S P, Cori, C F *Proc Soc exp Biol*, N Y

lition to the 30 proven cases of cœliac disease its were found to have a similar urinary amino matogram containing the substance correspond thanolamine phosphoric acid 5 were infant 1 month of age of whom 4 had erythroblastosi of these 4 3 received an exchange transfusi bsequently developed obstructive jaundice Th it had failed to thrive and had had loose motions as an adult—a man, aged 42 who died following tive jaundice

siblings of children with cœliac disease and 4 were suspected of having cœliac disease but boratory confirmation or adequate investigation was dwarfed and had lienteric diarrhœa began to vomit and failed to thrive at 9 month and a girl aged 8 years who had had repeated refused further investigation regarding steator

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nent of Child Health,
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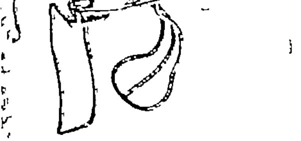
## New Inventions

### DIFIED MORSON BLADDER RETRACTOR

ULATION inside the bladder is often made by the posterior wall falling forward The on shows a modification of the Morson bladder which gets over this difficulty In the standard the middle blade moves in two planes only—forwards and backwards and from side to side; having a ratchet put in where this blade joins



it can be swung through quite a large arc in dotted lines) and the posterior wall of the can be retracted well out of the way

out subjects the Morson retractor seldom lies and it may become misplaced or even fall out bladder cavity With the modified instrument dle blade can be acutely angled so as to prevent pening Where the bladder is large and lax, etraction can be obtained by placing a swab the blade between it and the bladder wall

odified version of the Morson retractor was made for e Endoscopic Instrument Company Ltd London.

Maurice Lee
M.D Durh., F.R C.S

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## Reviews of Books

### Medicine in its Human Setting

*Being Clinical Stories for Students Nurses and Practitioners*
A E. Clark Kennedy, M.D F.R C.P physician, The London Hospital London Faber & Faber 1954 Pp 276 13s 6d

Here is one more 'guide to practice'—clinical original stimulating and eminently palatable It is addressed to students, nurses, and practitioners, and can be read as a set of vivid clinical lectures describing the onset, symptoms, signs, recognition, management and course of many common and significant system diseases and functional disorders. The emphasis is on observation recognition of clinical pictures simple remedies, common sense, and humanity The limits, no less than the scope, of our knowledge and powers are justly indicated The stories will stand the student in good stead in his finals if his examiners are the clinicians they should be; and they present an illuminating picture of practice and the practitioner Anyone intending to go into general practice and also any new-generation specialist, who wants to know what a good family doctor is asked to do how he does it, and what help he needs from his hospital and from his colleagues will find it here Flaws are rare: is there really still 'no treatment for hypertension' and is not heroin outmoded even for those with secondaries in their bones? The book's value is unquestionable and Miss Treadgold's lively drawings adorn and point the tales.

### Hæmatological Technique

E M Darmady M.D Camb F.R.C.P senior pathologist and S G T Davenport F I M L.T chief technician Portsmouth and Isle of Wight Area Pathological Service London: J & A. Churchill. 1954 Pp 107 18s

This book is primarily designed as a class book for medical technicians wishing to pass the examinations in the hæmatology section of the Institute of Medical Laboratory Technology Though it makes no mention of the techniques concerned with blood-groups which form an important part of the syllabus it covers all the other techniques and it endeavours at the same time to give a brief explanation of the fundamental mechanisms behind the disease process Here however, the difficulties of compression have sometimes defeated the authors and some of the explanations—e g in the section on blood coagulation—are confusing The various cells met with in blood and bone-marrow films are illustrated by single examples shown on colour plates which are well done and carefully reproduced The various hæmatological techniques are fully described and the advantages and disadvantages of each are clearly set out There are one or two omissions—e g the popular method of estimating hæmoglobin by means of a photoelectric instrument—but what is more upsetting is that there are so many evidences of perfunctory proof correction names wrongly spelt wrong initials, incomplete sentences and so on Such slips are readily corrected by those familiar with the subject but the book is not designed for them For the technician or for the medical student this first edition is disappointing—the more so because the publishers have shown that it is possible to produce a book with 4 colour plates at a very reasonable price

### Legg Calvé Perthes Syndrome

*And Related Osteochondroses of Youth* Charles Weer Goff M.D., assistant clinical professor of orthopædic surgery Yale University School of Medicine in association with Ned M Shutkin M D Springfield Ill: Charles C Thomas Oxford Blackwell Scientific Publications 1954 Pp 332. 77s 6d

Dr Goff gives us the fruit of some fifteen intensive investigation into what is most referred to as Perthes disease in this country

Making full use of his training as a physical he has endeavoured to assess the type to this disease Following Keith and epiphyses into three sorts

He considers that only the first variety—i e, those involved in joints—are liable to "true osteochondroses," and he refers to such lesions as Schlatter's disease of the tibial tubercle or Sever's apophysitis of the os calcis as "false osteochondroses" The latter group is seen in normal well grown children, but "true osteochondroses occur in a genetically conditioned individual with evidence of depressed growth before and after onset" The condition is more or less restricted to the White and Mongoloid races, and in over 20% of his 103 cases there was a definite hereditary factor

As far as immediate ætiology is concerned, he cannot go further than say that "the fundamental pathogenesis in the osteochondroses and in L C P S in particular is an occlusive vascular phenomenon resulting in bone necrosis" Whereas trauma is the essential factor in the false osteochondroses, he feels that it is no more than a common precipitating cause of the appearance of Perthes' disease He believes that the hip escapes this disease before the age of two because it is only at that age that full extension of the joint with resulting increased liability to strains is acquired He describes the treatment on a frame which he follows at Newington and suggests that there may be a future for growth promoters, he has tried aureomycin in this connection with, he believes, some improvement in his results He does not mention the lipoid dystrophies in connection with the ætiology of Calvé's disease of the spine, which he looks on as a true osteochondrosis

This is a thorough and painstaking piece of work, beautifully produced It is not always easy to read, however, the text would gain greatly if short words replaced those apparently chosen for their length

### Fundamentals of Psychoanalytic Technique

TRYGVE BRAATOY, M D, late head of the psychiatric department, Ullevål General Hospital, Oslo New York John Wiley London Chapman & Hall 1954 Pp 404 48s

THE late Dr Braatøy was primarily concerned, in this book, with psycho-analytic technique from what might be called the amateur's standpoint—as a means of investigating and understanding the patient developed to the level of an art

Braatoy was born in Minnesota, of Norwegian parents, obtained his medical training in Oslo, and then studied in Paris and at the Psycho analytical Institute in Berlin under Dr Otto Fenichel He later returned to the United States, and this book was written while he was training analyst at Topeka He thus had an unusually varied background and analytic training His approach was predominantly psycho somatic, and his general medical interest in his patients' bodily symptoms was obviously one of his main therapeutic weapons—a feature in which he greatly resembles the young Wilhelm Reich He is well grounded in orthodox Freudian psycho analysis, but his refusal to be limited by what he regards as unnecessary shibboleths enables him to supply a useful corrective to the too cerebral approach of some orthodox analysts These, indeed, may demur at some of his views, but they and all psychotherapists must find much to sympathise with, or to make them think anew

Every good physician will enjoy this book for its warm humanity

### Stellate Ganglion Block

*Techniques–Indications–Uses* DANIEL C MOORE, M D, director, department of anesthesiology, Mason Clinic, Seattle Springfield, Ill Charles C Thomas Oxford Blackwell Scientific Publications 1954 Pp 280 75s

IN this monograph dealing exclusively with the stellate ganglion and its infiltration by anæsthetic agents, the anatomical variations of the ganglion are well illustrated with full-scale drawings, and its physiology is colourfully, if sketchily, mentioned

Probably the most satisfactory chapter deals with the injection technique for stellate ganglion block, the methods used by Dr Moore are clearly presented and he also describes—perhaps with unnecessary generosity—33 alternative methods He states that some fifty diseases are benefited by single or repeated stellate ganglion blocks, but he does not present adequate experimental evidence for this, and few people in this country would accept it as satisfactory therapy for scleroderma, thrombo angiitis obliterans, livedo reticularis, or the cervical rib syndrome— a few of the conditions mentioned. Indeed th for stellate ganglion block are extremely few, the hard core of this monograph could have satisfactorily presented in a short paper

### The Lowenfeld Mosaic Test

MARGARET LOWENFELD, M.R.C.S London Neame 1954 Pp 349 144 coloured test car

To Dr Lowenfeld belongs the credit of described the technique now known as ph used for the diagnosis and treatment of th logical disturbances of children With her she must have been one of the first to empl nique of "projection," but she has only available a full account of her material an particular application of the method It is p leading to call any projection technique and certainly, in Dr Lowenfeld's hands, material goes further in diagnostic and procedures than any mere test The phenomena she calls attention are of great psych but the reader may not feel sure that she has every one of her conclusions He may appointed that the book does not give him using the "test" for himself

The book is well produced and it is accompa coloured reproductions To have these separat text is not particularly convenient, but sin combinations of them—twenty or thirty at needed to illustrate each chapter it is hard to see solution could be found

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**The Story of Medicine** (London Hutchin Pp 343 21s)—This history of medicine, wri layman by Mr Kenneth Walker, F.R.C.S, will b interest, for it is well written and well illustrated of the doctor has always had a fascination for the some of the greatest contributions to medicine made by amateurs Many striking examples given Leeuwenhoek, the Dutch draper, saw home made microscope what no other man had before, a whole new world of micro-organis Mary Wortley Montagu, the wife of our am Turkey, did pioneer work for the prevention o The Rev Stephen Hales, by means of ingen experiments, threw light on blood pressure. E the book the clergy are shown in unfavourable they often used their pulpits in an attemp progress

In the first part of the book the medical men chiefly responsible for them are given in c order as a connected and sweeping history, but rise of specialisation, Mr Walker abandons this a series of excellent chapters recounting the specialty This unfortunately makes his story fusing, for we read of blood banks, isotopes, and before we read of anæsthesia and antisepsis Even Pasteur's experiments on immunisation are describ before we reach those on Jenner, and the work of before the recognition of the cause of puerpe which preceded it by twenty years. The read shocked here and there There is the story of and handkerchiefs infected with smallpox were North American Indians—an undoubted form of logical warfare He may also be left wondering wh of our current therapeutic methods may not be future histories of this type

**Whitaker's Almanack 1955** (London Whitaker 15s)—This year's issue is as big as last year's has sixteen pages of photographs, the Royal tour place of the Coronation Two photographs show Bannister winning a mile race in less than four Oxford and at Vancouver There is a new s Defence, and new tables show the revenue and of Scotland separately from those of England, wise this invaluable compendium is much the those engaged in a race for factual information on reaching the right page in considerably less minutes

THE LANCET

NDON  SATURDAY, FEB 12 1955

## armacology of Chlorpromazine

ROMAZINE has been the cause of lively sy since its introduction into therapeutics [2] Largely this is because some investigators the unusual properties of this drug to sustain s of their own making Thus LABORIT [1,2] long been seeking a pharmacological method ing complete autonomic blockade during anæsthesia, hailed chlorpromazine as a tative disconnector DECOURT [3] studied is of chlorpromazine in many species in the d vegetable kingdom and reported that it ique mode of action, to which he gave the arcobiotic" Some of the early clinical ors described imprecisely the changes by the drug Thus it was said to cause l lobotomy or "chemical adrenalectomy a was made of its supposed specific effect n undefined symptom tension ion of chlorpromazine that is now well under ts antagonism to naturally occurring neuro substances Chlorpromazine has little sm to histamine [4-6] acetylcholine [4,6-8] nor o,[4-7,9] or cholinesterase [4] but by contrast powerful antagonism to adrenaline [4-7,9-11] tle or no ganglion blocking activity [5,7,8,10] respects it resembles dibenamine [7] and nolytic compounds This powerful specific ic action of chlorpromazine may account lity to protect against traumatic and hæmor ock, for dibenamine phentolamine and renolytic compounds are very effective—chlorpromazine is—in preventing shock experimentally in animals [12] Much ty might be dispelled by repeating with enolytic drugs the laboratory and clinical ts undertaken with chlorpromazine There sonable doubt that chlorpromazine exerts fects When this drug is added to a slice n a Warburg flask the oxygen consumption in cells is reduced [4,13] This is significant, ame thing happens with many drugs which y lack the other actions of chlorpromazine itioned reflex is induced in rats by teaching limb a rope on the ringing of a bell, the tion of chlorpromazine leads to a state stimulus of ringing the bell no longer the response [4] But not all the nervous traversed by this reflex are known and the site and mode of action cannot be deduced. The effects of chlorpromazine can be studied on other reflex arcs the anatomical pathways of which are more accurately known For example, chlorpromazine may sometimes cause hypotension in man [14] and similarly in animals, if the central end of the cut agus is stimulated the blood pressure rises and this rise can be prevented by *prior administration of* chlorpromazine [4,15] This blocking effect may be due to the peripheral adrenolytic properties already described or it may represent a true central effect The arguments for central action have been strengthened by evidence that chlorpromazine lowers blood pressure when administered in amounts that do not block the pressor effects of adrenaline The injection of minute doses intracisternally into rhesus monkeys causes a fall of blood pressure and blockade of the carotid pressor reflex, whereas the pressor response to the systemic injection of adrenaline remains unaffected [15] Granted that this hypotensive action is 'central' what is its precise site and mechanism ? The hypothalamus and medulla of the cat are known to contain areas direct or reflex stimulation of which produces a rise of blood pressure [16] *If these areas are stimulated in the* decorticate cat to which chlorpromazine has been administered in a dose too low to exert a peripheral adrenolytic effect there is no pressor response [18] This seems to indicate that chlorpromazine can *depress the activity of hypothalamic* and medullary centres with specialised autonomic activity, but the effect can be demonstrated only in conditions so grossly unphysiological that it would be unjustifiable to infer that it reflects events when the drug is administered clinically

There is need for more detailed characterisation of the central effects of chlorpromazine perhaps along the lines successfully pursued in the investigation of reserpine [17], and reports of such work are beginning to appear [18] A second need is for the clinician to become his own pharmacologist defining precisely *the effects of the drug There are welcome* signs from controlled clinical trials of chlorpromazine in psychiatric patients [19,20] that the psychiatrist is aware of this need The problems of the pharmacology of a drug are partly the problems of the physiology of the tissues where it acts and much of our uncertainty about the actions of chlorpromazine stems from imperfect knowledge of the integration of the central nervous system

## Nutritional Cirrhosis

THERE are several reasons for suspecting that uncomplicated nutritional deficiency is not alone responsible for the high incidence of hepatic cirrhosis in many malnourished communities The correlation between cirrhosis and malnutrition is not as close as would be expected from observations in laboratory animals The state in animals is not strictly comparable with that in man for whereas in animals on deficient diets the distribution of fat is centri

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H Huguenard, P *Pr méd* 1951 59 1329
H Huguenard P Alluaume R. *Ibid* 1952 60 206
I L. *Thérapie* 1953 8 840
ker S., Fournel, J., Ducrot R., Kolsky M., Koetschet *int Pharmacodyn.* 1953 92 305
J *C R Soc Biol., Paris* 1954, 148 192.
J, Armitage, A. K *Brit J Pharmacol* 1954 9 390
o I *Arch int Pharmacodyn* 1954 98 303
I L., Brunaud M Brunaud, S *C.R Soc Biol.* 953 147 100
A., O Mullane F J Gaskell P Churchill Davidson, ancet, 1954 ii 614
er M, Vogt, M *Brit J Pharmacol* 1954 9 402.
iberghe J., Hoebeke, A Milhied G *Arch int Pharma* 1954 98 341
Z. North, W C Well J A *J Pharmacol* 1954 112,
L., Fornl, R. H *Pr méd* 1953 61 1165

[14] Rea, L I., Ebes, J Fazekas J F *J Amer med Ass* 1954 156 1219
[15] Dasgupta, S R. Werner G *Brit J Pharmacol* 1954 9 389
[16] Werner G *Ind med Gaz* 1953 88 111
[17] Tripod J., Bein, H. J., Meier R. *Arch int Pharmacodyn* 1954, 96 406
[18] Das N N, Dasgupta, S R., Werner G *Ibid* 1954 99, 451
[19] Elkes J., Elkes C. *Brit med J* 1954 ii 560
[20] Anton-Stephen D *J ment. Sci.* 1954 100 543

lobular, in patients with kwashiorkor it is periportal, and such patients, unlike malnourished animals, are resistant to choline and methionine The inadequacy of malnutrition as a full explanation of the gross variation between hepatic disease in different parts of the world is especially well illustrated in a report by WALTERS and WATERLOW[1] on fibrosis of the liver in West African children in the Gambia

A survey of the food habits of the people in this area leaves no doubt that malnutrition is a major factor in their lives, their daily calorie intake ranges from 1570 in April to 1980 in December—shortly after the rice harvest, when the daily intake of protein (almost entirely of vegetable origin) does not exceed 50 g Fatty infiltration of the liver was not common at any of the ages studied—namely, from early infancy to 20 years The prevalent hepatomegaly could not, therefore, be attributed to fatty infiltration, and since the incidence of fibrosis in the symptom-free group of children with hepatomegaly was about the same as in the control group without hepatomegaly there is no justification for regarding this hepatomegaly as a precursor of cirrhosis, comparable with the large fatty liver in the rat From the low prevalence of fatty infiltration of the liver, in contrast to findings elsewhere—for example, by WATERLOW[2] in the West Indies—it must be concluded that the diet, despite its obvious deficiences in both quality and quantity, was not lacking in lipotropic factors Positive toxic agents, such as bush teas, which are at present suspected as the cause of the peculiar type of fibrosis reported from the West Indies by HILL et al,[3] do not seem to be involved But the exceptionally high incidence of parasitic infestation demands attention Malaria, which affects 62% of infants in their first year, almost every child by the age of three, and 20% of adults, is undoubtedly the most serious form, but helminth infestation runs it close The rôle of malaria in the genesis of cirrhosis has long been debated, and, although there is no convincing evidence that it can itself cause cirrhosis of the Laennec type, many competent observers have reported increased portal cellularity and portal fibrosis for which no other cause could be found WALTERS and WATERLOW point out that this type of hepatic fibrosis was especially common in the Gambia in the first few years of life, when the incidence of malaria is at its peak, and they are inclined to accept a causal relationship With regard to the diffuse type of fibrosis, which resembles Laennec cirrhosis much more closely, the relationship with malaria is less evident, in the age group in which this form of fibrosis is common, the incidence of malaria has fallen considerably If the relatively low intensity of malarial infestation in these older children and adolescents induced the fibrosis, then this should have a far wider geographical distribution corresponding to that of endemic malaria

Neither malnutrition nor malaria, therefore can be held to account for the severe hepatic fibrosis in the older Gambian children But it is conceivable that what neither does alone may be done by both together, and WALTERS and WATERLOW suggest that in fact, at least in the Gambia, the of malaria and malnutrition accounts for t In support of this hypothesis they m troversy as to whether the primary involved the parenchyma or the They suggest that malaria produces sli to the connective tissue, resulting in scarring, this damaged connective tiss sensitive to stimuli that tend to evoke response, and slight parenchymal injur an otherwise normal liver would be complete healing, in the malarial scarred l increase in the pre existing scar tissue a cirrhosis This attractive unifying hy not yet been substantiated experimental

The rarity of severe fatty infiltration in these Gambian children is noteworthy parts of the world where a similar diet severe fatty infiltration is common. In unlike the West Indies, the over all caloric diet is low This is of the greatest the requirement of lipotropic agents is to the total caloric intake In labo which the lipotropes are restricted so suffice to maintain the liver fat at a a supplement of sucrose is as deleterious caloric amount of alcohol[4], either lead fatty infiltration and cirrhosis These res cal observation and of experiment em vulnerability of people living on diets Toxic agents, mild infections, dietary modifications harmless to the well nourished may, prove catastroph protein deficient

## Splenic Circulation

THE splenic circulation has been two methods The first consists in dissection, injection, and histological e spleens removed at operation or necrop second in transillumination of the livin small animals such as the mouse D centred on whether the splenic circulation or "open" In the supposed "closed" there is a direct pathway through vessels sizes from artery to capillary, venule, munication with the pulp spaces taking through the capillary walls In the suppo type of circulation the capillaries are tho into the pulp spaces and the venules to from these spaces, perhaps via the in venous "sinuses" in which movement MCNEE[5] and KLEMPERER[6] put forward a hypothesis This was that capillaries were in direct continuity, but at some junction area "pores" or spaces allowed tion and interchange of cells and plasma vessels and the interstices of the pulp tree has two unusually constructed area interchange might take place One is at "ellipsoids" These are elliptical sheaths the penultimate part of the terminal the wall is composed of endothelium is about 5 μ, the capillaries extend only a ance beyond the ellipsoid. The other likely the splenic sinuses These form a plexus mosing vessels with peculiar walls, which to **Klemperer**, are composed of longitudin ated endothelial cells arranged in a ridge er and surrounded by anastomosing reticular xperimental evidence of the existence of was provided by **Björkman**[7] who showed e rabbit spleen particles of up to a certain ass through the blood vessel walls into the s while larger particles pass on to the veins mal is exposed to infection or to the action tic antibodies, particles five times as large gh to the pulp, so the size of the pores h circumstances

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[1] Fibrosis of the Liver in West African Children By J H WALTERS and J C WATERLOW *Spec Rep Ser med Res Coun, Lond,* no 285 H.M Stationery Office 1954 Pp 71 8s 6d

[2] J C *Ibid* 1948 no 263

R. Rhodes K Stafford J L Aub R *Brit med J* i 117

[4] Best C H Hartroft, W S, Lucas, C C., R 1949 ii 1001

[5] McNee, J W *Lancet*, 1931 i, 951

[6] Klemperer, P *In* Handbook of Hemat vol 3, p 1 H Downey New York, 1938,

f the most striking work on this subject was **Knisely** From direct transillumination of the living mouse he concluded that the rculation was entirely closed[8] Later e et al[9] pointed out that observations ely's technique could equally be interpreted g that the circulation was completely open ial capillaries opening into the spongework enic pulp which in turn drained into the uses **Whipple** and his co workers[10] have rted results obtained with an improved for studying the circulation in the spleen ng mouse Their findings suggest that the els are connected in several different ways The afferent arterioles lined by m are distinguished by the rapid blood flow em Some of them end in curious funnel npullæ (originally described by **Thoma**) oles are linked with capillaries that may ty directly into the pulp spaces or connect ith venous channels in addition some riovenous anastomoses were observed The et from the pulp spaces from the sinuses arterial vessels directly, and they empty to larger collecting veins **Whipple** now ether the sinuses exist separately at least onal sense he thinks that they are simply us channels in which the flow is sometimes o they can drain from or empty into the s. The pulp spaces themselves are com gular and have no endothelial lining, the through these spaces is also irregular may be stationary for long periods, and on of flow changes often, through the blood cells appear to wander quite at The pulp receives blood from the ampullæ rioles from capillaries directly, and from empties into veins The direction of the in the pulp and in the smaller veins depends ressure differences in the various parts of ommunicating system The flow is also the fact that the larger white cells often smaller channels sometimes the block is l, and then plasma and platelets pass but re held back. From these observations and his colleagues now put forward the conclusion that everyone is right—that both "closed" and "open" systems exist side by side in the spleen.

All these experiments were necessarily done on small animals—mice and rabbits But there is indirect evidence of a similar state of affairs in man Thus the well known microscopic appearance of the spleen in congenital spherocytosis shows that the red cells pack the pulp and compress the sinuses so there must be channels for their egress from the arterial side while their entry into the veins seems to be less easy **Atkinson** and **Sherlock**[11] have shown that the pressure recorded from a hollow needle passed into the splenic pulp is an index of portal venous pressure so there must be free inter communication between the pulp spaces and the portal venous system The evidence from splenic venography is even more striking **Dreyer** and **Budtz Olsen**[12] pointed out that the injected opaque medium leaves the spleen very rapidly—so rapidly that the first X ray film must be exposed as the injection is being completed and a second only three seconds later This too surely signifies free communication between the pulp spaces and the venous outlet even if there are some "closed" channels as well **Dreyer** and **Budtz Olsen** noticed that injected diodone does not diffuse throughout the whole spleen, it is limited to one "compartment" that drains into one of the hilar splenic veins The half-dozen or so main branches of the splenic artery do not intercommunicate to any great extent and this accounts for the liability of the spleen to infarction

Many hypotheses about the ætiology of diseases associated with splenomegaly assume that in some of these blood-cells get out into the pulp and are held there, while in others back pressure along the splenic veins leads to distension and dilation of the venous passages in the spleen A mixed closed and open system would allow this sort of thing and it is useful to have confirmation of such a system from both physiology and pathology

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## Annotations

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### URINARY EXCRETION OF ŒSTROGENS

In seeking to differentiate endocrine disorders resulting from hypersecretion or hyposecretion of androgens the clinician can rely on valuable help from the biochemist but not so with disorders due to abnormal ovarian secretion In the absence of a practicable chemical method and conscious of the tedium and uncertainty of biological assay most clinicians have taken the vaginal smear as a simple if rough indication of the events of the œstrous cycle But now the Edinburgh school by developing two independent methods for assaying urinary œstrogens[13, 14] have made possible the systematic study of ovarian function This success is the outcome of hercu lean effort. During the menstrual cycle the daily urinary output of œstrogen (13–60 μg) is less than a hundredth of the corresponding androgen level and the isolation of the three compounds—œstradiol œstrone and œstriol—which is a pre requisite for their determina tion by the chemical method represents an over all purification of one in more than five million

Biological assay measures total activity but does not identify the compounds contributing to this activity; whereas the chemical methods isolate the known urinary œstrogens, all of which have different biological activity If it is assumed that œstradiol, the most active compound, is the genuine hormone, then the determination of the relatively inactive metabolites, œstrone and œstriol, may give a misleading impression How far such determinations reflect the œstrogenic activity of the endocrine glands is not certain Comparison of 17-ketosteroid levels in plasma and in urine has revealed substantial differences[15], these differences imply a degree of selective renal clearance, which has thrown some doubt on the value of urinary 17-ketosteroid determinations as an indication of androgen secretion From the pattern of œstrogen excretion throughout the menstrual cycle, it is clear that urinary œstrogen levels follow the events of the ovarian cycle remarkably closely Dr Brown's study of a representative group of non pregnant women, reported on p 320 of this issue, has confirmed the existence of two peaks of excretion, one corresponding with ovulation and the second with maturation of the corpus luteum All three urinary œstrogens show this cyclic variation, with a sharp drop immediately after ovulation, but the absolute and relative amounts vary considerably between different cases In competent hands the method is fully reliable, but because of the differences in secretion between different women, and in individual women according to the stage of the cycle, isolated determinations are valueless—and such a determination will represent ten hours of work wasted

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[7] E. *Acta med scand* 1917 128 suppl 191
[8] H *Anat Rec* 1930 65 23 131
[9] D W Jun, Whipple A O Wintersteiner M P *Anat* 1911 48 397.
[10] O Parpart A K Chang J J *Ann. Surg* 1951

[11] Atkinson, M Sherlock, S. *Lancet* 1954 i, 1325
[12] Dreyer B., Budtz Olsen, O E. *Ibid* 1952 i, 530
[13] Bauld W S *Mem. Soc Endocrin.* (in the press)
[14] Brown J B *Ibid* (in the press).

Definition of the normal limits of secretion is a necessary preliminary to the study of abnormal conditions The opportunities offered by this development are great, but the inherent difficulties should not be forgotten one microgramme is the twenty-eight millionth part of an ounce

## LUNGS, BONES, AND JOINTS

THE clubbed fingers of Hippocrates are commonly regarded[16] as a localised form of the more widespread "hypertrophic pulmonary osteo-arthropathy" of Bamberger[17] and Marie[18] Clubbing usually accompanies the bony and soft tissue changes of hypertrophic osteo-arthropathy, and in some cases of apparently "simple" clubbing radiography of the long bones reveals new subperiosteal bone Clubbing and ossifying periostitis are often accompanied by symptoms of joint disease For the whole complex Marie's title can appropriately be altered to "generalised hypertrophic osteo arthropathy,"[19] since the associated systemic disease is not invariably pulmonary In general the clinical implications of simple clubbing and of the complete picture of hypertrophic osteo arthropathy are similar, but Hansen[20] found that the latter was particularly likely to develop in patients with a localised lung lesion, such as carcinoma or abscess

Wierman et al,[21] at the Mayo Clinic, found finger-clubbing in about 5% of cases of malignant tumours of the lung submitted to resection, and the joints were painful in less than a third of these Arthralgia without clubbing was rare Like Ray and Fisher,[22] Wierman et al found clubbing in a higher proportion of cases of bronchiectasis and lung abscess, but no patient had painful joints Clubbing was extremely rare in pulmonary tuberculosis The curious association of articular manifestations with pleural mesothelioma[23] was fully arthralgia was the initial and predominant 7 of the 14 cases of this uncommon tumour analysis it appears that a patient with sever which has preceded the development of cl or the discovery of symptomless patholog lungs or pleura, is likely to have either a p thelioma or a malignant pulmonary lesion, is no clubbing of the fingers mesothelioma probable diagnosis Several workers[24-27] attention to cases of malignant disease of which prominent or even presenting fe suggested rheumatoid arthritis (for examp spindling of the fingers, effusions into j erythrocyte sedimentation rate) or rheumat and Fisher found that 10% of cases of carc lung had acute osteo arthropathy, with pa the initial complaint In nearly all such cas was at the periphery of the lung

The pathogenesis of hypertrophic osteo has not yet been satisfactorily explained generally ascribed to peripheral anoxia or of endocrine function rather than the "toxi workers Reduced pulmonary aeration se to play a part in those cases of bronchogen where only a small volume of lung is invol which pneumonectomy may rapidly cure pathy But peripheral arterial anoxia may suggested, be due to alterations in the sta cell suspension Mendlowitz,[28] having dem increase in digital blood-flow and a de brachial-digital arterial pressure in simp (which was absent when bony changes w thought that the clubbing might be a c response to altered circulatory dynamics changes were found in congenital clubbing of dyspituitarism as a causal factor, Fried four cases in which acromegalic features de hyperplasia of the eosinophilic cells of the p observation which recalls the distinction of osteo-arthropathy by separation from acro presence of gynæcomastia in some cases of altered endocrine function The regre resection excludes stimulation of the pituita tases within its substance[30] as a common The high incidence of arthropathy in pleural and in peripheral lung tumours suggests th may in some way be concerned. Hansen[20] nervous reflexes from the lung[31] played a p cited the curative effect of hilar neurectomy resection Finally there remains unexplain of cases in which hypertrophic osteo-arthr accompanied by any demonstrable prim The disease usually starts in boys at p adolescence, and it tends to progress slow deformity and sometimes extreme disabilit is thought to be distinct from hereditary which periosteal proliferation may occur very extensive

From the work of Gall et al[19] it seems th hypertrophic osteo arthropathy is most first the distal third of the forearm and leg ends of the humerus and femur, and later

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15 Migeon C J Plager J E *Recent Progr Hormone Res* 1954, 9, 235
16 Locke E A *Arch intern Med* 1915 15, 659
17 Bamberger E *Wien. klin Wschr* 1889, 11, 226
18 Marie P *Rev Médecine* 1890 10 1
19 Gall E A, Bennett, G A, Bauer, W *Amer J Path* 1951 27, 349
20 Hansen J L *Acta med scand* 1952 142 suppl 266, p 467
21 Wierman W H Clagett O T McDonald J R *J Amer med Ass* 1954 155 1459
22 E S, Fisher H P *Ann intern Med* 1953 38
23 Clagett O T, McDonald J R., Schmidt H. W 1952, 24 213
24 Craig J W *Brit med J* 1939, i 760
25 Van Hazel, W *J thorac Surg* 1940 9
26 Holmes H H, Bauman E, Ragan C. 9, 169
27 Mauer, E F *Amer Heart J* 1947, 34
28 Mendlowitz M *Medicine Baltimore* 1942, 21
29 Fried B M. *Arch intern Med* 1943 72,
30 Bloom W *Ann intern Med* 1948 29 361
31 Wyburn Mason R *Lancet*, 1948 i, 203.
32 Camp J D Scanlan R L *Radiology*

l metatarsals—a pattern which should be kept hen seeking radiographic confirmation of the Others have reported changes in the clavicle tella, iliac crests nose and malar eminences teum thickened and infiltrated with lympho down new bone matrix on the underlying ecially over extensor surfaces Tendon inser go metamorphosis into fibrocartilage which is ced by bone forming intratendinous osteo y resorption the original cortex becomes can l in time can no longer be distinguished from bperiosteal bone In the joints there is chronic with degenerative changes in the articular there may be hypertrophy of villi and a pannus ' may even form The subsynovial œdematous and infiltrated with lymphocytes ı-cells In the terminal phalanges there are onal spur like overgrowths of bone and the o largely confined to the soft tissues The ndles of the corium are swollen and the extra ues infiltrated with round cells Pain and in the joints are probably due more to arthritis jacent periostitis

## E OF TUBERCULOUS PATIENTS BY AIR

wledge of the special problems involved in g invalids by air is based largely on hard won in war time, when air evacuation of casualties mes a tactical necessity as well as a means ife. Investigators at that time were particu ated in the effect of altitude upon traumatic rax and their observations have since been good effect in the conveyance by air of patients with artificial pneumothorax and itoneum For example the British Overseas rporation have since 1951 flown more than ts to and from sanatoria in Switzerland, and of the arrangements on these flights has now by Dr Peffers [1] assistant director of medical O.A C

with moderately severe pulmonary tubercu ad received little or no previous treatment, d on the outward flights Very advanced with severe impairment of lung function, ith pleural effusion or recent severe hæmop onsidered unsuitable, either on the grounds twelve months sanatorium treatment in was unlikely to be of much benefit to them the risks of the journey were adjudged too the patients returning to Britain some had al pneumothorax or extrapleural collapse noperitoneum and some thoracoplasty in disease had been stabilised but resection erformed at a later date All the patients the care of the Department of Health who were responsible for initiating the

ft employed were Argonauts pressurised at erential of 4 12 lb per sq in Thus while y flew above the weather at about 15 000 assengers were subjected to a reduction in ion and pressure not greater than is experi 00 feet—the altitude of the Swiss sanatoria me the principal disadvantage of air travel es which arises from the fact that air in or peritoneal cavity obeys Boyle s law and under reduced atmospheric pressure causes spiratory embarrassment and may result g of adhesions. It was recommended that pneumothorax or pneumoperitoneum should a refill in the week preceding their flight ; mediastinal fixation was suspected the lung had to be at least three quarters expanded at the time of travelling Of the 1300 patients only 3 showed signs of respiratory or cardiac distress 1 had a bilateral artificial pneumothorax, and responded well to treatment with a cardiac stimulant and oxygen while the other 2 recovered quickly with rest.

To prevent air-sickness all patients were given hyoscine hydrobromide gr $^1/_{150}$ one hour before take-off An incidental effect of this drug and one which in these cases was obviously desirable was to reduce secretion of sputum Several oxygen cylinders were carried on each flight in case of emergency as well as supplies of stimulants and analgesics and apparatus (sterilised and ready for immediate use) for performing pleural puncture in the event of the pressure in an artificial pneumothorax becoming excessive

Rigorous precautions were taken to prevent contamination of the aircraft s furnishings and fittings All food-containers utensils and cutlery were destroyed after use sputum flasks were issued to each patient wash hand basins and toilets were disinfected after each flight and as soon as the passengers had disembarked, the interior of each aircraft was sprayed with 5% formalin being later washed down with soapy water and a strong disinfectant Two doctors—one supplied by the Scottish health department and one by B O A C—were in attendance on each flight and the stewardesses were required to have hospital nursing experience All aircrews were volunteers contact between them and the patients was kept to a minimum and as an additional safeguard the flight-deck and cabin crews were radiographed at six monthly intervals

Thus in these charter flights great care was taken to protect the patient and to prevent spread of infection Patients with open tuberculosis must not travel on scheduled flights lest both they and others be exposed to hazard

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[1] rs A. S R. *HBA Bull Edinb.* 1954 12, 59

## HYPERPARATHYROIDISM AND PEPTIC ULCER

SINCE we last discussed the differential diagnosis of hypercalcæmic states in adults [1] two American reports have emphasised the difficulty of distinguishing primary hyperparathyroidism and the syndrome of hypercalcæmic renal failure from excessive intake of milk and soluble alkalis by patients with peptic ulcer [2] Carpenter and Pautler [3] describe a case in which there was a clear history of excessive milk intake without ingestion of soluble alkalis and without increase of serum bicarbonate necropsy showed that the condition was due to a solitary parathyroid adenoma Kyle [4] compares two apparently similar cases One of these was a true example of the milk alkali syndrome ; the patient who is said to have taken up to 3 litres of milk and 220 g (2700 m eq ) of sodium bicarbonate daily died of uræmia and necropsy revealed severe nephrocalcinosis. In the other case the patient also gave a history of excessive milk and alkali intake but a calcium infusion test [5-7] gave a result more suggestive of primary hyperparathyroidism (i.e , an increase rather than the normal fall of urinary phosphate) and complete clinical cure followed removal of a solitary parathyroid adenoma The co-existence of hyperparathyroidism and symptoms of peptic ulcer in these two cases is not a chance happening Over twenty years ago Gutman et al [8] showed that hyperparathyroidism was often associated with anorexia, nausea, vomiting, constipation, and epigastric pain, and that the symptoms could easily be confused with those of duodenal ulcer Rogers et al [9, 10] first described the actual association of the two conditions, and many striking series have since been reported Howard et al [11] stated that 15% of all cases of hyperparathyroidism diagnosed at the Johns Hopkins Hospital were complicated by peptic ulceration. Hellstrom,[12] reporting a series of 50 cases of hyperparathyroidism, pointed out that 5 of the 17 males and 2 of the 33 females had duodenal ulcer St Goar [13] has recently described experience at the Massachusetts General Hospital, where, of 137 patients with hyper parathyroidism, 12 had a proved peptic ulcer and a further 5 had very suggestive dyspeptic symptoms Although hyperparathyroidism is two and a half times as common in females as in males, of the 12 patients with proved peptic ulcer 8 were males and 4 were females From these reports there is little doubt that the incidence of peptic (usually duodenal) ulceration is greatly increased in males with hyperparathyroidism

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[1] *Lancet* 1954 i 91

[2] Burnett C. H Commons R. R Albright F Howard J E *New Engl J Med* 1949 240 [illegible]

[3] Carpenter H M Pautler E J *Ibid* 1954 250 453.

[4] Kyle L. H *Ibid* 1954 251 1035

[5] Howard J E, Hopkins T R Connor T B *J clin Endocrin* 1953 13 1

[6] Kyle L. H Schaaf M Erdman L. A *J Lab clin Med* 1954 43 123

[7] Nordin B E C, Fraser R *Clin Sci* 1954 13 4

Gutman, A B , Swenson, P C , Parsons W B *J Amer med Ass* 1934 103 87

This complication is even more prominent in an uncommon hereditary endocrine disease which includes hyperparathyroidism Underdahl et al [14] described 8 patients with multiple endocrine adenomata in the pituitary, parathyroids, and islet cells of the pancreas, 3 of whom also had a peptic ulcer Wermer [15] describes a family in which the father and 4 of his 9 children were affected, in 4 of these 5 cases peptic ulceration was also present

Rutishauser and Majno [16] found that injections of large doses of parathyroid extract in normal dogs produced œdema and necrosis with calcification of the deeper portions of the glands of the gastric fundus Simultaneously there was a sharp rise in serum-pepsinogen levels, indicating increased leakage of the enzyme into the blood stream When peptic ulcer complicates hyperparathyroidism, the kidneys are more liable to be affected than the skeleton Increased calcium intake from the high-milk diet usually prescribed in peptic ulcer tends to prevent excessive demineralisation of bone, but leads to severe hypercalcæmia with nephrocalcinosis or renal calculi Parathyroidectomy often cures the complicating peptic ulcer as well as the hyperparathyroidism

## CHEMOTHERAPY AND SURGERY IN PULMONARY TUBERCULOSIS

FIFTEEN years ago Dolley and Jones [17] undertook the first deliberate operative removal of tuberculous lung tissue For a decade thereafter confidence in the procedure steadily increased, but only in the past five years has resection swept into favour This change, which could hardly have taken place without chemotherapy, has been hastened by dissatisfaction with the older methods of treating some forms of pulmonary tuberculosis —for example, fibrotic bronchial stenosis, destroyed lung, large tension cavity, and tuberculoma

The hazards of resection have considerably diminished Francis,[18] reviewing the first 100 partial resections at Harefield Hospital, found that, whereas 90% of patients who had had round foci removed did well, of those with more serious disease only 64 satisfactory result and no less than 20% bronchopleural fistula In many of these ca patients received no chemotherapy, and given less than 20 g streptomycin. The a adequate chemotherapeutic preparation is the results lately obtained by Thompson et Hospital of 266 resections (including 118 tomies) only 8 (3%) resulted in fistulæ.

Owing to chemotherapy many patie submitted to resection with the disease in a decade ago would have been regarded a indeed, it becomes more and more difficult, apparent effectiveness of chemotherapy, to cases should be operated on Such doubts n as sometimes happens, the resected lung sho slight evidence of active disease, even ca converted into apparently inert cysts P monds,[20] describing such a case, observe guishing feature of the cavity wall is a com ment of caseous and tuberculous tissue by ordinary granulation tissue, in which foreig cells are conspicuous" Clearly, should healing prove usual and permanent, the in pulmonary tuberculosis would be slight, and Simmonds point out, incomplete regarded as the more probable outcome they still advocate collapse or resection for of relapses, and resection in most cases of have healed as cyst like spaces, which secondarily infected, distend, or even cases collapse therapy scarcely seems ade besides, complete healing of cavities diagnosed with certainty before operation.

Present-day thoracic surgery is thus influenced by chemotherapy Temporary as pneumothorax and phrenic paralysis, fall out of favour, but pneumoperitoneum widely practised as an interim measure and ment to chemotherapy in patients unsuitab More resections are being done, but on a conservative scale, with more segmental fewer pneumonectomies On the other clinicians still hold that collapse therapy resection—though the evidence for this, yet conclusive There is great need for a statistical comparison of the two perhaps the present large scale inv surgical operations by the British Tuber tion and the Society of Thoracic Surgeon fill this gap

## NEW ANALGESIC

ASPIRIN has given many years of satisfa as an analgesic and antipyretic drug alternatives have been continually sought facture of salicylic acid by what is known Schmitt reaction, a "brown dust" is residue One constituent of this is 4 hydro acid, which has been subjected to prelimin logical study [22] Acute and chronic toxicity and mice show that the substance is not and it has analgesic properties Clinical tr progress

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Prof E D ADRIAN, O.M., P.R S, on w was conferred in the New Year honours, t title of Baron Adrian of Cambridge

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# Social and Biological Factors in Infant Mortality *

## OBJECTS AND METHODS

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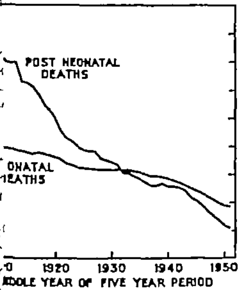
per describes the background and plan of an to the 80 000 stillbirths and infant deaths urred among the 1½ million children born in nd Wales during 1949 and 1950 The informa ned when these deaths were registered is the information obtained when the children were born 'Biological' factors such as the mother's age and the number of her children and social factors such as the father's social class and occupation and the part of the country and the type of community in which the birth took place are thus related to the deaths to their certified causes and the ages at which death took place All these factors nnected Social factors for instance act through biological factors affecting the size of family g of children the nutrition of mother and child pportunities for infection In turn biological he size of family most obviously—profoundly a social situation; moreover as in the complica regnancy or the viability of infants born pro they are differently effective in different

Clearly, therefore, the various factors will understood in theoretical terms if they are gether as well as separately This is necessary al grounds too since any particular factor f factors, may offer opportunities for preventive The present inquiry attempts such a many roach to the problems of infant mortality



ar trends in neonatal and post-neonatal y in England and Wales in 1906–53.

al' refers to the first four weeks 'post-neonatal' to the rest of ar Unless otherwise stated the in this paper refer to all births multiple illegitimate and of both

* * *

ant mortality rate in England and Wales has four fifths in the last fifty years from over 150 and births in 1900 to less than 30 today The of infant death moreover is now different in ell as in size from what it was at the beginning ntury Deaths in the *first four weeks of life*— deaths—contributed 66% of all infant deaths in 1953 in 1906 (separate figures for the neonatal period are not available before 1906) 68% of the deaths were *post neonatal* —in the *remainder of the first year of life*[11] Whereas the post neonatal mortality rate fell in the period by 90% the neonatal rate fell by less than 60% (fig 1) The decline in the infant death rate after the age of 4 weeks is similar to that in the mortality of young children generally (fig 2)

The relatively much more rapid drop in the *post neonatal* death rate has been due in large measure to improved infant feeding and to the reduction of infectious diseases the main outstanding problems today being infections of the respiratory tract. *Neonatal* mortality, on the other hand, is dominated by 'immaturity' of the infant and physiological failures by injury during birth by congenital malformation and by mechanisms leading to 'asphyxia' and 'atelectasis' These processes are little understood if at all and the results of new treatments have been less dramatic The underlying causes of these deaths in the first month of life and particularly in the first week (during which the great majority of the deaths in the first month occur) are similar to those of stillbirth; and there is an increasing tendency to consider stillbirths and deaths in the first week as a single problem such terms as 'perinatal'[10] or 'obstetric'[9] deaths being used to describe them With changing problems the emphasis in current research is thus shifting to the antenatal period and the circumstances of the birth to the study of mother and child together and to factors which affect the vitality of the child through the mother Such influences are the more likely to be effective the shorter the infant's life until in stillbirths they must be predominant It is possible, moreover that some of the underlying causes of the numerically greater problem of abortion before the 28th week of pregnancy (the arbitrary stage after which the term 'abortion' is not officially used) may be similar to those of stillbirths—but even less is known about this problem.

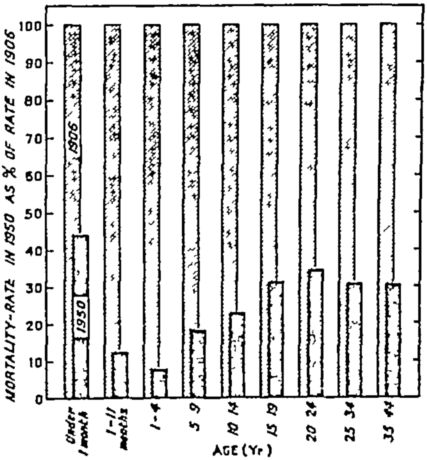


Fig 2—Decline in mortality at different ages in England and Wales from 1906 to 1950

Mortality rates per 1000 live births in first year; per 1000 persons living at other ages.

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f articles reporting an inquiry made jointly by the Medicine Research Unit (Medical Research Council) the General Register Office The articles were pre by the Unit in collaboration with the General ter Office and have been approved for publication joint working party responsible for the inquiry

## Social Factors

It is a commonplace of the study of infant mortality that social influences are at their strongest in the post-neonatal period, related as they are to infection, but it does not follow that their effect on the *stillbirth and neonatal death rates* is negligible There is a step-by-step increase in both these rates from social class I to social class V in the scale, based on the occupation of the father, which is used by the General Register Office[37] † The rates of death attributed to prematurity—one of the most important considerations in perinatal mortality—are similarly affected[41] The incidence of premature birth, defined by weight, in a national sample was higher (6 6%) in the children of manual workers than in those of professional workers (4 3%)[8 23] In Aberdeen in 1949–51, premature births were twice as common in social classes IV and V as in classes I and II[3] The babies of parents living in the poorer districts of Birmingham are not so heavy, on the average, as the babies of parents living in the more prosperous districts[10] Moreover, there are marked and consistent differences between different towns and regions of England and Wales in their stillbirth-rates, and in their neonatal mortality-rates, also These differences are of the familiar kind, with high rates in Wales and the industrial North of England

How the social influences affect the stillbirth-rate and neonatal death-rate is not at all clear It is noticeable, for instance, that the stillbirth-rate, which had changed little from about 40 in 1928, began to fall rapidly in 1940–41, and reached 23 in 1948—at about which figure it has since persisted (fig 3)[38 39] Duncan, Baird, and Thomson[9] have concluded, from detailed inspection of the trends, that national food policy contributed much to the decline which took place in social classes III, IV, and V in the later years of the war, and which was particularly noticeable in deaths associated with prematurity, for example Neonatal mortality also fell rather more rapidly after 1940 (fig 1) However, in spite of a more homogeneous national diet,[28] social class differences in stillbirth and neonatal rates in 1949 (fig 4) were relatively as large as in 1939, and so were many local and regional differences in these rates Stillbirths and infant mortality in other countries, with very varied war time experiences, have also fallen substantially during the same period[30] This consistency suggests that other factors besides nutrition were also concerned in the general fall, which must be studied in the context of the great decline in infectious diseases, and of other mortality trends of recent years

The rôle of diet has been taken as an example of the difficulty in distinguishing the various factors responsible for differences between the infant-mortality rates of different groups in the population We shall not here discuss the numerous paper with these factors, but the following im ences, amongst others, have been studied differences in family size, class differences quality of maternal care, work in pre mother's education, availability of antenat specialist medical services, the relative ad domiciliary and hospital confinement, ho tions, and climatic differences[2 3 20 23 25 31] useful distinction can be made between, on th those factors affected by current money inc food and, on the other hand, those more expenditure on "capital assets," such a education—changes in the latter being slo effect[27] It would be true to say, however, th two factors mainly responsible for the social ences have been identified Meanwhile, fa problem in as long a perspective as pos and peace, slump, recovery, and boom The

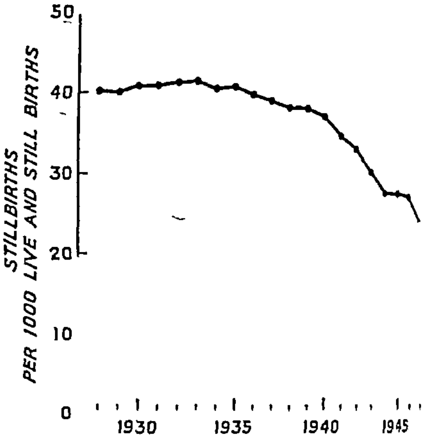

Fig 3—Secular trends in stillbirth rate in England and

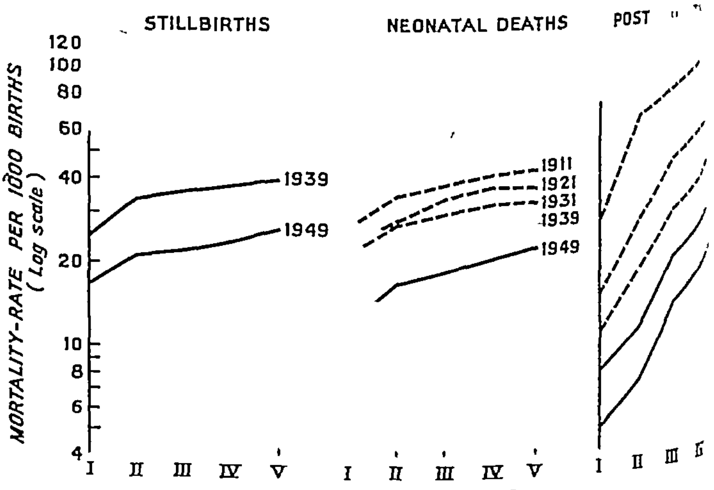

Fig 4—Social-class differences in stillbirth, neonatal, and post-neonatal mortality-rates Wales in 1911–49

Stillbirth rates per 1000 live and still births, other rates, per 1000 live Rates for 1911 are adjusted compared with published figures because in classification All data refer to legitimate births

social class I and social class V shows no signs in spite of much recent levelling in their and more than forty years of health service differential impact—a truly remarkable history

### Biological Factors

The effects of the biological factors in infant mortality are perhaps less genera

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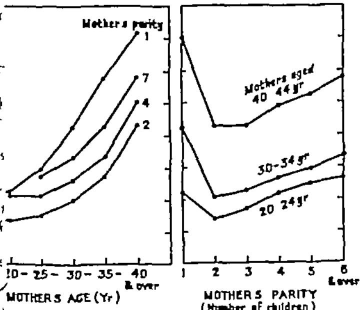
† Examples of the allocation of occupations to the social classes

| *Social Class* | *Description of occupations* | *Examples* |
|---|---|---|
| I | Professional &c | Physician company director |
| II | Intermediate | Farmer shopkeeper |
| | illed workers | Coal face worker most clerks |
| | skilled workers | Machine minder, most agricultural workers |
| | workers | Railway porter builders labourer |

formation is slowly accumulating on these al processes of human biology A brief— sarily inadequate—summary of the main ws.

position that *maternal age and parity* ar in the outcome of a pregnancy is well recognised of the experience of the elderly primipara, le—her liability to toxæmia and to unexplained and premature birth the increased risk of bour and birth trauma. Many other relation recognised clinically such as the association h fertility with twinning and with maternal and of *parity* with birth weight with the of antepartum hæmorrhage and of rhesu nplications The main patterns of variatio tillbirth rate and neonatal death rate with age and parity were first put on a sound basis by Yerushalmy [48, 51] and a number of dies have followed [1, 4, 26] The stillbirth rate with the *mother's age* for a given number of fig 5) and the increase is sharper after 30 When the variation with the *number of* considered, for mothers of given age the rate r first births, falls sharply in second births rises steadily thereafter (fig 5) The neonatal re not so clear and will be discussed in a later



ation of stillbirth-rate, with mother's age and parity for tion single legitimate live and still births in 1939–50.

s of these biological variations it has been that the differences between the stillbirth he social classes are not much affected by the the professional class for instance, contains more elderly primiparæ ' who are subject risk of stillbirth or by the fact that social thers are younger on the average which tends their rate Whether such class differences and parity of the mothers affect the neonatal neonatal rates has yet to be shown and is the the third paper in the present series

ork still needs to be done on the relation of age y to the individual causes of stillbirth and ath Baird, Walker and Thomson [5] have 1000 stillbirths and deaths in the first week of occurred among booked cases in the Aberdeen Hospital during the period 1938–52 in terms ognised pathology and the age and parity of rs (They found, it may be mentioned that of the neonatal deaths were due to conditions nfections arising *after birth*) In about one all the cases no cause could be postulated, hese being prematurely born In about 10% attributable to maternal toxæmia which was important in the youngest and eldest primi ntepartum hæmorrhage accounted for another 10% Trauma during birth was responsible for 20% of the deaths and these deaths were specially common among the older mothers with primigravidæ worst affected Deformity led to the deaths in 15% of the total McKeown and his colleagues in their detailed studies of congenital malformation, found considerable differences in the way that individual defects were related to maternal age and parity, though first birth and relatively advanced maternal age are never favourable factors [19, 19, 21, 22, 24] That such factors are related to *deaths* from congenital malformation at all is of course interesting, if they are related to *incidence* as McKeown's studies suggest this is further evidence of the importance of the fœtal environment These findings provide a link with the work of Gregg [13] Ingalls,[14] and others on the effects of ' insults to the growing fœtus The reports of the Registrar General for Scotland [40] give data on the variation of the rate of stillbirth from several broad groups of causes by maternal age and parity

The variations of the death rates (chiefly the stillbirth rate) with *other biological factors* (multiple birth, interval between births, sex of infant &c) have been dealt with by various authors Some of the more important findings in the literature are

(i) The male stillbirth and infant-death rates are higher than the female rates; the ratio of male to female stillbirths increases with the age of the mother [15, 22, 24]
(ii) The ratio of males to females for all stillbirths for macerated fœtuses, and for anencephalus increases with duration of gestation.[17]
(iii) Stillbirths and infant deaths due to different congenital malformations show different sex ratios For example only about a quarter of stillbirths with anencephalus are males less than a quarter of infant deaths due to congenital pyloric stenosis are in females [22, 46]
(iv) Like sexed twins have a higher stillbirth rate and neonatal death rate than unlike-sexed twins.[16, 33]
(v) Neonatal death rates are much higher in multiple births than single births Stillbirth rates as a whole are also higher in multiple births than in single births; but the reverse appears to be true for fœtal deaths occurring before the 28th week of pregnancy [21, 46]
(vi) Multiple births occurring in the youngest mothers show a very high stillbirth rate This rate falls with the age of the mother to a minimum at 25–34 years and thereafter rises sharply again—in contrast to the rate for single births which shows no such early fall [16, 33]
(vii) Women who have had stillbirths are particularly likely to have further stillbirths those who have lost a *child in the first four weeks of life are particularly* likely to do so again; and the same is true for post neonatal deaths.[40]

There is an association between congenital mal formation of the central nervous system in one child in a family and abortion stillbirth and similar malformations in its siblings.[23]
(viii) There are indications that the spacing of births may influence the *stillbirth* rate and *neonatal death* rate very close spacing and very distant spacing may be disadvantageous.[4, 41, 45, 50]
(ix) There is a suggestion that consanguineous marriage may increase stillbirth and infant mortality rates.[11]
(x) Stillbirth rates and neonatal mortality rates are higher for the children of younger and older fathers compared with those aged 25–34; and this holds independently of the relationship of the rates to the *mother's age* [51]

For deaths occurring after the first few weeks of life there is no information based on large numbers relating to the effects of maternal age and parity or of the other biological factors (except the infant's sex) The available evidence [4, 6, 11, 35] suggests that the influences of age and parity in the post neonatal period differ from their effects on the stillbirth and neonatal mortality rates.

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### The Present Inquiry

The present inquiry which is an epidemiological exercise in the vital statistics of infant mortality the documents of birth and death registration of England and Wales, and for the first time brings them together  Information about the mother's age, the number of her children, the duration of her marriage before the birth, and whether the birth was single or multiple, is obtained at birth registration (but not for the public record), while other data, such as the age of the infant, and the cause of death, are obtained when the death is registered  Information on the social circumstances surrounding the birth or death, such as the father's occupation, the community in which the family lived, and the infant's legitimacy is also available  All this material will be brought together for the two years 1949–50, and for the whole of England and Wales  Since similar information for stillbirths was easily available at the same time they are also included in the inquiry  In addition, mortality in the second year of life of children born in 1949 is being studied

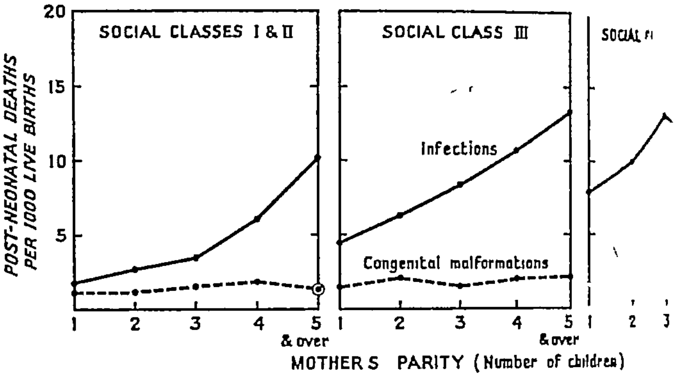

**Fig 7—Variation, with parity, of post-neonatal mortality from infections (different social classes compared) for single, legitimate births in Englad**

Ringed plotting point is based on less than 10 deaths

There are several problems on which it is hoped that the inquiry will provide useful information

The influence on the death rates of the *mother's age*, and *the number of children* she has borne, will be examined in a variety of social circumstances  It will be possible to say, with some certainty, for instance, whether the increase in the stillbirth-rate associated with a first birth is greater for the wives of unskilled workers than for those of professional men, whether the infant-mortality rates for social class v are high because of their larger families, and whether the rates in the North of England are higher merely because there are more people in social classes IV and v there than in the south ‡  This analysis will be made for the deaths occurring at various ages during the first two years of life, and particular attention will be paid to the "perinatal" period of greatest risk

The next step will be to investigate whether maternal age and parity have different influences in relation to the different certified *causes of death*  Deaths from and with "prematurity" are a leading example  Unfortunately there are serious difficulties in interpreting the causes of infant death as given on death certificates,[24] and the data will therefore fall short of the standard expected in good clinical practice—with all that may remain in this  However, what is l logical precision may, it is hoped, be made ways  An example of some of the questio present analysis will raise is shown in fig The more children there are in the family the post-neonatal death rate from infection, wi seems to be no such association of famil deaths from congenital malformation (taken at this age, and these observations apply in social class groups  Moreover it is the co young mother and large family that seems to matter  The demonstration of such rel peculiarly within the scope of an epidemiol such as this—which thus adds something clinical study cannot provide  Again, some precision of the data about causes will be reference to the presence of a post-mortem and by separate study of deaths taking place Thus it will be possible to analyse almost from congenital malformation, confirmed b and to relate the anatomical sites of d if only in broad terms, to the age of the number of children she has borne, any loss children, and so on  No information is inquiry about the *causes* of stillbirth, either maternal disease or of fœtal pathology history of vital statistics confirms that analy categories, such as "stillbirth," can be while

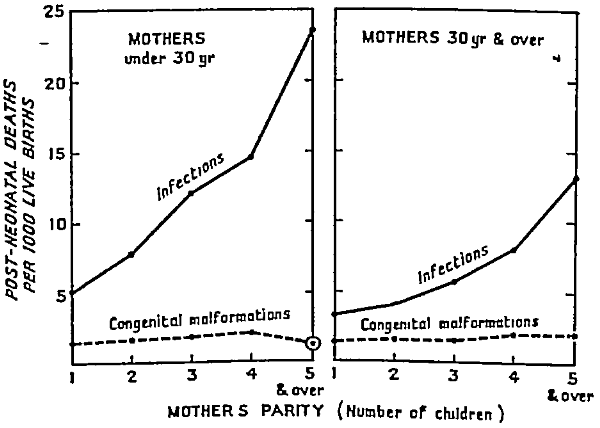

**Fig 6—Variation with parity, of post-neonatal mortality from infections and congenital malformations (younger and older mothers compared) for single, legitimate births in England and Wales in 1949**

Ringed plotting point is based on less than 10 deaths

As mentioned earlier, *birth spacing* may b affecting the death rates  The inquiry, by infant mortality in terms of duration of ma the mother's parity, can contrast the infa rate for women who have had a large numbe in a short married life (and therefore in rapid with the rate for women who have had few a long married life, the two groups of w matched for the contingent variables of age class  This is an indirect, and rather a blu but it is difficult to get any information st subject  It will also be possible to study mortality rates for women having their first b soon after, and a long time after their mar possible implications about the relations mother's fertility to subsequent infant loss

An association has been mentioned b occurrence of stillbirths and infant death *loss of previous children by the same mother* Th ness" to lose children will be examined in va of mothers, and evidence sought whether so death (e g, congenital malformation, or "pr not further defined) are more responsible t ely it will not be possible to trace the causes 1 ages at, death of the previous children formation is available about the mother's tory apart from the fact that she has previously d number of children

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‡ As at present progressing the inquiry is less concerned with "climatic" factors, though it is hoped to remedy this later

blems will be investigated because the present approach provides the opportunity and then 1 the circumstances to explore The contrast e effects of the mother's age on *single and* llbirths has been mentioned. The present ll examine the neonatal and post neonatal among children of single and multiple births contrasts (Fig 8 shows for instance that death in the first four weeks of life is of the e in six for multiple births to women under cing no correspondingly high risk for single ese very young mothers ) Again it has been stillbirth rates and neonatal death rates are ng *like sexed than unlike sexed twins* Is this death rates in the next eleven months of ct genetic inquiry is beyond the scope of the dy ) Further, the *excess of male over female* ncreases *with mother's age* *Is this true also* ortality ?

present inquiry deals only with the documents tistics study of the *social factors* which it sible to make is strictly limited. No direct will be available for example on patterns ire and other aspects of family behaviour, gical influences or even on such elementary family income and expenditure. Very little ained on the hundreds of thousands of life- receding the events being examined The us will be mainly in terms of the grading of tion (mentioned before) into five social used by the General Register Office in the tables. This does not provide a *classification* als on the basis of their personal circum er than occupation and it is thus in some ude and ill-defined Nevertheless, since its n forty years ago it has proved the most strument for social medical research in this er) country The allocation of mothers and social class is by father's occupation, and upation groups are being studied as well as ses The number of these, however is limited l considerations and those selected will broadly exemplify ways of life as well as sible to deal with specific problems Miners, for instance have been chosen for special study because their infant mortality experience in the 1930s was particularly unfortunate Was this due only to their special poverty[24] in the inter war years? One of the lesser objects of the present inquiry is to yield some hindsight ' on such questions, by analysis of the contemporary (and, in this instance very different economic) situation In the present inquiry the facts about the father's occupation are taken from the birth record both for the dead children (since the records of birth and death are now linked) and for the live births which *form the basis* ( *denominator* ') *of the infant* mortality rates Hence it is possible in line with the aims of the inquiry to concentrate on the circumstances of the birth In addition there is no error comparable to that which occurs in adult occupational mortality rates when the information about the death appears on a different document, and refers to a different time, from the census information about the ' population at risk

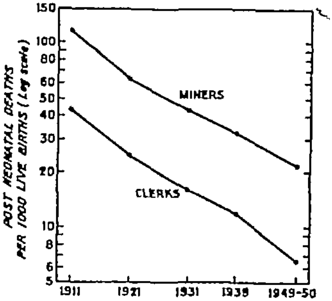
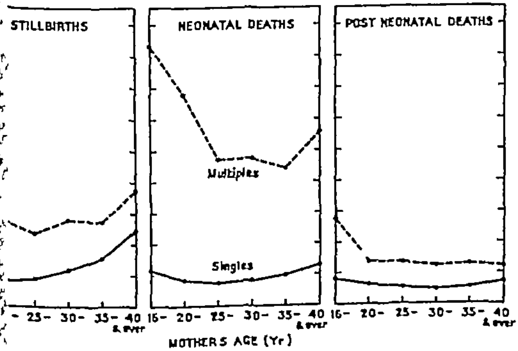


*Fig 9—Secular trends in post-neonatal mortality of children of miners and of clerks in England and Wales in 1911–50. (Legitimate births.)*

The inquiry as a whole was designed of intention—and *necessity—to be close to the 1951 census and it is pro*posed to make as much use as possible of the social data that will become available from the census. Information on school leaving ages in various occupation groups will be used as an indicator of educational level and more remotely of culture patterns in different groups similar information will also be available for various geographical areas. In addition, considerable use will be made of the census information on housing conditions and amenities in different towns and different parts of the country The classical studies by Farr Simon, Newsholme, and others of infant mortality in relation to the physical environment and the micro-climate will thus be brought up to date in a small way vis à vis the changing family composition changing standards of living post war housing problems and increasing urbanisation and suburbanisation—and the low infant mortality rates achieved in recent years The unexpected uniformity in the fall of the stillbirth and infant mortality rates in the five social classes (fig 4) will *be further explored in terms of the* experience of particular occupations such as miners and clerks (fig 9) and of different parts of the country Plans have not yet been made to study the varying social services of different communities in relation to mortality As a start, however the death rates will be analysed according to the place of confinement—at home in hospital or in a nursing home—having in mind the different admission policies in different



on with mother's age of the stillbirth and infant-mortality rates (single and multiple births compared) for legitimate births in England and Wales in 1949

rates, per 1000 live and still births other rates per 1000 live births areas "*Legitimacy,*" "*illegitimacy,*" and "*prenuptial conception*" are of course social concepts, and they have many associations with poverty, with type of community and educational levels, as well as with family upbringing and individual social experiences Moreover, the mothers concerned are younger, on the average, than married women, and more of them are having their first babies A study of the known unfortunate experience of illegitimate babies is therefore inadequate if it does not refer to these various factors[43]

Reference is made earlier to a division of factors into "*social*" and "*biological*" This classification was adopted mainly for historical reasons, for convenience, and (it is hoped) for clarity It seems useful to distinguish, where possible, "biological" factors, by which is meant factors such as the mother's age which have meaning whatever the social setting (they can be applied to other creatures, and, indeed, the influence of maternal age is well recognised by animal breeders), and factors, such as occupation, which derive their meaning from "social" organisation Certain factors, however, could be classed as "biological" from some points of view, and "social" from others duration of marriage, and spacing of children are both examples of this In the last resort social factors must act through the biological, though not necessarily the ones included in this inquiry, while the importance of the biological factors for preventive medicine lies in the degree to which they can, if indeed they should, be controlled by individual and community action It must be remembered that, so far as developing embryo and fœtus are concerned, all factors, however they have been described, are truly "environmental"—whence such hopeful notions as "antenatal pædiatrics"

## Opportunity and Method

The opportunity to carry out the present inquiry was provided by the Population (Statistics) Act, 1938 This Act, the main purpose of which was to collect material relating to fertility, was passed at a time of considerable public concern with the population trend It provided for the recording, under conditions of secrecy and for statistical purposes only, of the age of the mother, the number of previous children born to her, and the date of her present marriage, for every confinement in England and Wales from July, 1938, onwards Since then, therefore, the basic data for a study of the relationship between these biological and the more commonly studied social factors in infant mortality, and using national statistics, has been in existence Early in 1948, after a preliminary reconnaissance, the Social Medicine Research Unit suggested such an investigation to the General Register Office who agreed on a joint inquiry

*Numbers*

The inquiry is concerned in round numbers with the $1\frac{1}{2}$ million births which occurred in England and Wales in 1949 and 1950 (the "population at risk"), with the 33,000 of them which were stillbirths, and with the 44,000 or so where the baby died in the first year of life The opportunity will also be taken to study the deaths in their second year of life of the children born in 1949 there were about 1600 such deaths This makes a total of about 80,000 deaths and stillbirths to be analysed

*ic Document*

basic document used in this entirely documentary y is a special form which is completed by the local ar from *information supplied to him by the* informant" of a birth or death The actual birth and th certificates themselves are not used, because they not contain the data obtained under the Population tatistics) Act The place of residence of the parents, and other data such as the name of the child, its sex, and the place of birth, appear on the birth certificate, but details of the mother's age, her previous and the date of her marriage, do not For cause of death is given on his certificate by the practitioner, and is copied on to the form by the re who also enters on it other information, such a father's occupation, obtained directly from the

*Relating Births to Deaths*

The essential practical problem was to find which babies born in 1949 and 1950 died in infanc various relatively unsuccessful pilot trials in 1948 used different methods of tracing, a method was e which proved very successful in practice and depended on the war-time National Registration s The birth records *corresponding to 99 4% of the* reg deaths of the infants concerned were traced §

Having traced the relevant birth entry it remained for the General Register Office to record information about both the birth and the death on same form, and to punch machine cards from t sorting and tabulation

## Comment on Method

An essential element in this inquiry is that it "longitudinal" and "prospective" (? "prolept That is to say, it takes a set of persons (babies) observing the conditions which affect them at a time (birth), follows them all for a stated period attempt is made to assess the differing experience the present instance the numbers of deaths, and t causes) of children born in different circumstances social and biological This "cohort" approach can hav wide application in vital statistics For example, i might help to fill the often puzzling gap in our know when a good deal is known of the circumstances in wh a condition occurs, but little of why it selects some not others for its victims What is the previous med and gynæcological record of women who have premat babies, compared with those who do not? Or the medi and occupational history of men who subsequently develop coronary heart disease?[13] Attempts to obt *this kind of information retrospectively* often meet wit disappointment. A clear instance of the value of the "prospective" approach is to be found in the rece studies of smoking and cancer of the lung[7] The approach however, may be particularly expensive to apply, because in the nature of things a long period of observation may be necessary, and because a large cohort, few of whom will develop the disease, may need to be under continuous and uniform observation The opportunities for carrying out such work occur ideally, therefore, when the necessary data are being obtained as a routine for another—it may be administrative—purpose In the present investigation various statutory records in connection with the processes of birth and death registration were linked together for use in this way

A further point is that in this type of large scale epidemiological study it is possible, if only because of the numbers involved, to observe patterns and configurations of several "causes" or factors acting together, and at the same time more effectively to break down the combined action into some of the constituent elements What this means in practice can be illustrated from figs 6 and 7 These figures describe the combined effect of the three factors of social class, age, and parity in relation to deaths from infectious disease and congenital malformations All three factors, it is clear, influence the mortality from infections Considering, then, the two factors of age and parity, there are indications of a group of young mothers with large families who might well be paid special attention by the child welfare services trend of mortality with social class (alone) gives mise of a reduction in mortality rates from social rovements, whatever the age and size of family

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§ Emigration could have affected the validity of the rates, but a sample investigation showed that it did not Details of the method of tracing, of the 0 6% untraced, and of the emigration sample, will be given in the final report

* * *

## Conclusion

ifant mortality and stillbirths remain an important blem despite the great achievements of recent years. number of stillbirths in 1953 was almost 16 000 deaths in the first week of life some 10 000 in the mainder of the first four weeks about 2000 and th t-neonatal period 6000 The total of 34 000 was about , of all deaths, but because these deaths occurred at outset of life they represented considerably mor n 6% of the total wastage of life (in t[illegible] sonable expectation of years to be live[illegible] untimely deaths

The present inquiry will describe the [illegible] ge of mortality rates, and the lowest of [illegible] licate a goal which can be achieved in th[illegible] ite of medical knowledge ' Vulnerabl[illegible] th particularly unfavourable rates will be d[illegible] rious biological and social terms and [illegible] y thus indicate where and perhaps what [illegible] easures could be taken Moreover though [illegible] pproach is through infant mortality it is [illegible] pl preventive medicine that mortality repr[illegible] e tip of the iceberg of morbidity and the [illegible] pproach through morbidity and mortality [illegible] fruitful an approach as any to the practical de[illegible]tion healthy conditions The main contribution which pidemiology can make in our present ignorance of the mmediate intimate causes of stillbirth and neonatal nortality is to distinguish sections of the population vith high mortality rates and low so that underlying auses of mortality can be postulated These causes re likely to be general and non specific and they may ell offer opportunities for preventive action

We are grateful for the help of many people in this inquiry o members of the staff of the General Register Office at omerset House and in Southport for a very large share f the work and for their indispensable advice throughout o the Registrars-General of Scotland Northern Ireland the sle of Man, and Guernsey and the Superintendent Registrar of Jersey for help with the emigration problem; to Prof Dugald Baird Prof R M. Titmuss (who was an original member of the team) Dr Barnet Woolf and Dr A M Thomson for criticism and advice and to our scientific, erical, and computing colleagues, and particularly to Mr J Longdon, first statistician to the Social Medicine Research Unit who was in charge of the detailed work at the beginning of the inquiry

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# Medicine and the Law

## Negligence Appeal Fails

THE Court of Appeal have upheld the find Mr Justice Gorman[1] that the late Mr C A Jo [illegible] to perform an operation although suffering cancer at the time[2] The action had been broug Mrs Winifred M Nickolls against the Ministry of I [illegible] successors under the National Health Service . the liabilities of the Royal Free Hospital for neg performance of an operation for the removal of a [illegible] performed on her in December 1944

The plaintiff alleged that Mr Joll was then su [illegible] inoma of the lung and that he and the d knew or should have known that he was un [illegible] the operation As a result of it the pl [illegible] suffering from permanent bilateral rec [illegible] paralysis

[illegible] Justice Denning's judgment is of importa [illegible] profession His Lordship said that he [illegible] feeling that owing to Mr Joll's state of [illegible] or other went wrong in the operation [illegible] not be said to be negligence unless one [illegible] every time a surgeon was taken ill [illegible] theatre that would be negligence It w [illegible] or that Mr Joll was not paying atte [illegible] of that kind The real point was wh [illegible] should have undertaken the operation [illegible] very arduous and important task to oper [illegible] people and surgeons ought not to do it unles [illegible] do it But Mr Justice Gorman came [illegible] conclusion that Mr Joll was quite fit to pe [illegible] particular operation even though he was suf [illegible] cancer and the Court could not overrule the on the point The other lords justices concurre

Negligence actions must always turn largely o facts in each particular case Hence the judgme the present case do not lay down hard and fast but they do indicate general principles It now that it is not necessarily negligence to operate unwell but that *a surgeon should ask himself* fit to perform this particular operation?

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[1] *The Lancet* 1954 ii 58
[2] *Times* Feb 4 1955

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local authority hospitals (whatever their limitations may have been) were comprehensive For them the qualification for admission was need, whereas the voluntary hospitals which were groups of specialised units were concerned only about cases appropriate for treatment in these units The local-authority hospital undertook all the general duties left over

There are thus two main conceptions of a hospital (1) a comprehensive institution looking after the needs of human beings in a locality, and (2) a group of specialised units

It must be admitted that the comprehensive hospital has been out of favour since the introduction of the National Health Service Act, but there are some indications that the alternative has not proved entirely satisfactory The paper on Institutional Medicine, from the posthumous papers of Sir James Spence, which you published and commented on in your issue of Jan 1, stresses the danger of hospitals becoming mere "services" instead of "institutions" An institution is defined as "the establishment and arrangement of human effort towards a common end"

If the common end is the providing for the hospital needs of complete human beings it can be most easily reached by means of comprehensive hospitals Regard for the unspecialised needs of human beings was formerly one of the most important duties of medical superintendents It is disturbing to learn from the Bradbeer report that it is no longer considered to be a part of medical administration We read "it is primarily the matron and her nursing staff who create the comfort, the content, and the 'atmosphere' of the hospital and who can most influence the feelings with which the general public regard it The matron is the personal link between the community and the hospital"

I hope the medical profession will retrieve this duty as quickly as possible

The community in the main still consists of families, and it is difficult to dissociate the hospital needs of individuals from their family circumstances These needs can be most easily met by comprehensive hospitals Such hospitals should contain units for the main specialties, including an obstetric department with a closely linked pædiatric unit

Specialised children's hospitals will be advocated by university departments, and clearly they have some advantages for pædiatric education and research, but these activities, important as they are, are not the primary duties of the Minister in the hospital service

In any large hospital it is difficult to avoid undertaking the care of some children for various reasons if there is no pædiatric unit in the hospital, first rate facilities for treating them are unlikely to be present If there is a large children's hospital in a region there will be pressure to prevent the establishment of pædiatric units in the general hospitals Specialised children's hospitals are difficult and expensive to administer and usually have to struggle hard to maintain a sufficient nursing staff No doubt a case can be made for maintaining a few special children's hospitals, but I do not think they should be regarded as part of the normal pattern of the hospital service

Liverpool HENRY H MACWILLIAM

SIR,—Your annotation of Jan 29 draws attention to the general diminishing demand for children's beds

Many children's hospitals and children's wards were founded and endowed by people anxious to be of service to children They have been staffed by doctors and nurses imbued with the same tradition of service towards the child Their management committees are drawn from people with particular interest in the child While there is a need in the children's field it would be a misfortune to disband these sympathetic and generous forces concerned with the welfare of the child

I point to the lamentable need throughout the country for children's units for the inpatient treatment of the nervous child Pædiatric and psychiatric interest is focused more and more on this group of and clinical experience shows the need for the inpatient units, of which there are still very few country A small proportion of delinquent sometimes associated with emotional dist children are probably best dealt with elsewhe the greater proportion of emotionally disturbed can be adequately investigated with very little of present accommodation

Child Psychiatry Clinic
11 Fore Street, Ipswich J G

SIR,—It was with some misgivings that I in your annotation of the scheme to Princess Louise Hospital for Children to adult was in 1949 a resident at the other children's h the St Mary's group—Paddington Green—and I very clearly how a similar situation arose. At a medical committee, produced a plan for the of that hospital for adult E N T cases—a plan for its architectural infeasibility and disregard needs I hope history is not going to repeat precisely

Should, however, there now be real difficulty Princess Louise in keeping all its beds tenanted, I whether the idea has been considered of block of wards into a psychiatric unit for need for children's psychiatric inpatient care, to the places available, must far exceed the adult medical or surgical beds, great even as This scheme would at least have the advantage intact the character of the Princess Louise as a hospital, of giving a teaching hospital a unique in showing to its students cases of this kind, presenting an opportunity of linking more two rather estranged specialties of child psy pædiatrics

Maida Vale Hospital
Hospital, London, W 9 C H NEVILLE

## IMPOTENCE

SIR,—Dr Tuthill's article (Jan 15), while approach to the subject, does not explain how he treat acquired impotence where initially the was not impotent I should welcome his exp this on physiological grounds

Infertility Clinic, Victoria Memorial
Jewish Hospital, Manchester B SA

## GEOGRAPHY OF GENERAL PRAC

SIR,—As reported in your issue of Jan 15, the officer of health for Middlesbrough in his report seems to deplore that all the general p the town spend time motoring from one end of to another, and to suggest that this should be by the application of a nice tidy dose of admi medicine, confining certain doctors to certain and certain streets to certain doctors

Quite apart from the fact that such a step interfere with the freedom of choice of doctor, it not be too readily assumed that the few minutes driving in a car between patients' houses is wasted It affords the practitioner a few moments for re and relaxation (or, at any rate, a change of occup and, for those still uninhibited in the matter of a soothing cigarette It is, in fact, a sort of the practitioner's daily activity, and as such should be too hastily condemned

West Byfleet,
Surrey S J

## ISOBEL CRIPPS CENTRE

IN reply to Mr Neil (Feb 5), Dr Barlow writes "I sho- like to point out that one of the two advertisements I men- tioned appeared in a daily newspaper a few months ago, in 1950'

# Obituary

## ALBERT ERNEST HAMERTON

C.M.G., D.S.O., M.R.C.S.

nel Hamerton a former assistant director of gy at the War Office and for many years pathologist Zoological Society, died on Jan 31 at Brighton age of 81

father, the Rev Thomas Hamerton had a charge ls, and he was educated at Leeds Grammar School o University of Leeds. After qualifying in 1899 d the appointment of R.M.O at Leeds Public nary before joining the R.A.M.C In 1903 he was ted captain and the following year for his services action of Jidtalli in Somaliland he was awarded s.o In 1908 he was appointed to the Sleeping s Commission of the Royal Society and he worked e commission in Uganda and Nyasaland till 1914 m the beginning of the war he served in France rge of a cavalry field ambulance later at a casualty g station He was promoted lieut. colonel in 1917 ppointed C.M.G in 1918 While serving with the otamian Expeditionary Force from 1920 to 1922 s in charge of the Central Laboratory and Pasteur ute at Bagdad In 1923 he returned to this country ke up an assistant directorship at the War Office tired in 1928, and in the same year he was appointed logist to the Zoological Society

f Edward Hindle to whom we are indebted for culars of Hamerton s work at the Zoological Gardens, s out that he brought to his new post both a wide ience of medical research in many countries and nterest of a keen naturalist in the animals. The gical Society of London was the first organisation kind to make a practice of holding a necropsy on animal dying after being added to the collection annual reports from the prosectorium dating from middle of the last century are a valuable record of diseases prevalent in the collection and the eighteen rts by Hamerton are a mine of information He prepared a catalogued index of all the microscopical s of pathological specimens of animals brought to prosectorium in which the diagnosis of the cause death had been confirmed by at least two other rts besides himself

part from his routine work, his most important tribution was a study of the condition known as cage alysis which was first recognised in the London Zoo 935 This disease is confined to Old World monkeys was found to be the result of primary myelin degeneron of the spinal cord, with continuous demyelinisation he white matter from the cervical to the lumbar region showed that the disease seemed to be associated with ietary deficiency and responded to treatment with liver ract (*Brain* 1942 65 103) He also described another tal disease of monkeys, pulmonary acariasis, caused by a ite *Pneumonyssus simicola* infesting the lungs of captive ld monkeys. His other studies included the distribution tuberculosis among the animals and the diseases of ary birds. As a result of his work at the Zoological ardens he modified the views which he put forward the Royal Society s commission on sleeping sickness 1913 and no longer advocated the extermination of ld animals as a method of controlling the tsetse-fly le became convinced that in view of our limited owledge the destruction of big game was to be vored and he became a strong advocate of nature tion. Among all these activities he found time to ny institutions and research workers with e and anatomical and pathological material rium He finally retired in 1946

## ERT LISTER HORTON

S. Lond F.R.C.S. J.P

consulting surgeon to the Dorset the Weymouth and District at his home at Bournemouth o son of Dr Thomas Horton School in 1907 he entered the Bucknill scholarship College Hospital After holding houseappointments at his hospital he took the F.R.C.S in 1914 The same year, on the outbreak of war, he joined the Royal Army Medical Corps, and for his services in France as a surgical specialist he was mentioned in despatches. After the war he returned to University College Hospital as surgical registrar and tutor to dental students In 1920 he took the degree of M.S being awarded a gold medal

In 1922 he settled in general practice in Weymouth He also built up a surgical practice and joined the staffs of the Weymouth and District Hospital the Dorset County Hospital, Bridport Hospital and Herrison Mental Hospital During the late war military and civilian casualties greatly added to the burden of his work. These strenuous years told on his health and after the war he gave up some of his appointments and moved to Bournemouth But he continued work at Bridport and Herrison Hospitals until a few months ago He had been appointed a justice of the peace for Dorset in 1938

D J R S writes: Horton was one of a body of able men who between the wars, carried on the long-established tradition of good doctoring in south Dorset He was trained as a surgeon and he carried the promise of a brilliant student career into the full fruition of an extensive surgical practice His abundant energy enabled him to engage in a considerable amount of private general practice He was, thus, one of the diminishing band of doctors, unfettered by narrow specialism whose medical knowledge was truly wide and whose value to the community was thereby immeasurably enhanced His outstanding operative skill was based on full anatomical knowledge, beautiful hands and the judgment born of applied experience Every movement brought the end of the operation visibly nearer—there was no time for fiddling or showmanship We have lost a dear friend a man who never made an enemy His memorial will be enduring gratitude and affection in the hearts of the people of Dorset.

Mr Horton married in 1917 Miss Elizabeth MacDonald, R.R.C. She survives him with a son and a daughter, who is also a doctor

## GRACE MARY LUKOSE

M.B Lond B.Sc. Madras F.R.C.S.

Miss Grace Lukose, formerly assistant professor of surgery at the Lady Hardinge Medical College, New Delhi, died on Dec. 26 at the age of 39, after an accident

She first came to England in 1938 having graduated B.SC. at Madras University, and entered upon the second year of preclinical study at the London School of Medicine for Women, where her mother, Dr Mary Poonen Lukose who was surgeon general to the government of Travancore, also qualified

She graduated M.B. in 1946, after holding several unqualified house-appointments in which her aptitude for surgery became evident. On her return to India she worked at the Lady Hardinge Medical College New Delhi, for two years, and in 1949 she came to England on postgraduate study leave and lived at Canterbury Hall in Bloomsbury until she took her F.R.C.S. in 1951 Soon after her return to India in 1952 she was appointed assistant professor at the Lady Hardinge Medical College Last autumn she had a severe illness diagnosed as rheumatic fever from which she was making a slow but steady recovery She returned to her mother in Travancore, where in an attempt to help a relative whose hair had been caught in an electric fan she received the electric shock which caused her death

"It was during the years, writes K. M L. when she lived at Canterbury Hall, that many of us had an opportunity of recognising Grace Lukose s unique qualities and catching some of the gaiety of her infectious laughter Singularly free from any self-consciousness she quickly made friends and entered into every aspect of university life No-one could be more jealous than she was for the position and dignity of medical women nor more loyal than she to her friends and to the institutions to which she gave her affection

## Sir EDWARD MELLANBY

Prof H N Green writes of the personal qualities which made Mellanby a world leader in scientific medicine

He combined a powerful direct mind with an almost instinctive sense of what were the really important problems. Having decided on a line of research he astonishing zeal and single minded devotion which never flagged until the answer was obtained or was deemed unattainable I can recall so many such occasions, but one example will here suffice Before he left Sheffield he had become engrossed in studies on tumour respiration and the effects of toxic substances on it After leaving to live in London he and his wife came to Sheffield every weekend for several years to continue this work—the first train up on Saturday morning and the last back on Sunday evening, with the interval filled in assembling and recording the manometers of the Warburg apparatus

"Like most great seekers after truth he was essentially a modest man and all his achievements and honours sat on him lightly He only showed vanity, and that mainly in an impish sense, when in private he scoffed at those administrators who took the credit for health measures derived entirely from the arduous labours of medical scientists He always maintained that people with a gift for making discoveries should be given every facility to work as the spirit moved them and that directed research by committee ruling was a pompous waste of effort

"His greatest contribution to medicine was undoubtedly the impact of his nutritional discoveries on preventive medicine The discovery of vitamin D alone not only removed an outstanding cause of deformity but helped in the steady reduction in infantile morbidity and mortality Though he rarely commented on this, I think of all his achievements, this was the one which gave him the greatest quiet satisfaction

"For his dedicated life no one could have been more fortunate than Sir Edward in having such splendid help from his wife She took much of the laboratory and all of the domestic administration on her shoulders and was an active colleague in all his purely scientific work With all this she carried out extensive investigations of her own in which he played little part except that of admiring interest Her great companionship and zeal for work, equal to his own, was undoubtedly a big factor in his success, for it spurred him to effort over those dull patches of successive negative results which assail all investigators and sometimes make them flag The story of this lifelong scientific partnership is a grand one and perhaps some day it will be told."

Sir Arthur MacNalty writes

"When I became chief medical officer of the Ministry of Health in 1935, Edward Mellanby was one of the first people I consulted as to ways and means of promoting the ministry's medical work He did everything he could to help me, and the closer relations between the Medical Research Council and the Ministry date from that time Especially did I value his advice in promoting the Ministry's campaign for immunisation against diphtheria which has met with such remarkable success. On countless other questions he helped and advised When the second world war came, our consultations were more frequent and together we planned the Emergency Public Health Laboratory Service which was such a boon to national public health Later, at my request, he joined the editorial board of the *Official Medical History of the War*, and by his nomination of Dr F H K. Green and Sir Gordon Covell as editors of the volume on medical research enabled an adequate account of the council's war work to be recorded. I miss a true friend and a great scientist"

Sir Charles Lovatt Evans recalls that it was a surprise to many when "this sharp-spoken, quick-witted and able research-worker, who appeared to be somewhat of a recluse," was given the appointment of secretary to the Medical Research Council

"But under Mellanby's guidance," he continues, "the influence and achievements of the council developed enormously, and he grew with it He was a great man not only by reason of the distinction of his research work, but even more by his encouragement of the work of others. He had an amazing grasp of the multitudinous researches, and of the many research-workers under the council's ægis, and always remembered them, and had their interest at heart He was of wise counsel, shrewd in the appreciation of men, and forthright in the expression of his beliefs Not the least of his outstanding characteristics was the tenacity with which he continued his own research throughout the tenure of his heavy administrative position, working in his laboratory, with his wife, through the weekends to return, apparently refreshed, to his desk on Monday There can be no doubt that genuine devotion to his research was among the first things in his life"

## Prof JAMES WHILLIS

WRITING on behalf of the consultants, registrars visitors who meet at Stoke Mandeville Hospital Monday to discuss their problems of con reconstruction, and repair, T P K gratefully Whillis's monthly visits to the group

"Only illness or the pressing call of one of his other mural activities was allowed to cancel the visit, yet Mandeville Hospital, Aylesbury, is roughly forty mi west of London, and Whillis lived at Seal near Seven thirty miles south of the Metropolis It was a measure value he placed on these visits that he was prepared at the hospital mid morning and only leave to train via London with the expectation of reaching midnight These visits were to us a means of the right lines anatomically and functionally, and to link with the clinical applications of his specialty, with clinical matters in general Our apologies to his this imposition were always considered unnecessary she knew how much her husband enjoyed these visits would watch operations until lunch and spend the afternoon in the clinic where outpatients and inpatients freely and fully discussed To these discussions he contributed much sage advice and his presence invigorating as a breath of fresh air If time allowed he round off the session with a "lecturette" on some subject of our choice before we carried him off to dine in Aylesbury, hear one of those yarns he told so well, reluctantly see him to his train

"Everyone who met Whillis was fascinated by his b (almost puckish) outlook, all who knew him develope him a deeply affectionate regard He had many friends surely no enemies We shall remember him as the man the articulated finger bones in his pocket, always rea demonstrate the disturbances of function so commonly in the burnt finger, and as that rare teacher who could anatomy live and embryology understandable We shall on remembering (and missing) him in a thousand and ways, but most of all for his warm and loyal friendship."

## Appointments

BARTLETT T T M.R.C.S S.H.M.O, Mount Pleasant Ho Chepstow
FENTON, G I M B Belf., F R C S.I consultant orthopædic headquarters in Londonderry
NIGHTINGALE, DOREEN, M.S. Lond, F R.C.S consultant th surgeon University College Hospital, London
POLLOCK, MARGERY A., M.B Dubl F F.A R C.S, D A con anæsthetist, South Belfast H.M C
ROBERTSON, J D, M.D Edin M.R C.P E. F F.A R C.S, D.A. time consultant anæsthetist regional pool of anæsth based on Royal Infirmary, Edinburgh

**South-Western Regional Hospital Board**

BARNETT A F, M D Lond, M R C.P senior medical r Plymouth clinical area
GORDON, ALEXANDER, M.B Edin. registrar, departm pathology, Frenchay Hospital, Bristol
VILLET D DE G, M B Cape Town, F R.C.S surgical r Gloucestershire Royal Hospital, Gloucester

**Welsh Regional Hospital Board**

DAVIES D G H, M.R.C.S, F F.A R C S D A consultant thetist Newport and East Mon H.M.C
JENKINS R E, M B, D P M asst psychiatrist (S.H Morgannwg Hospital, Bridgend
JONES G MARTIN, M R.C.S senior casualty officer, St Tydfil's Hospital, Merthyr Tydfil.
JONES J G P, M.D Lpool M R.C.P, D C H. deputy m superintendent (S H M O) Llangwyfan Hospital Denbigh.

**Colonial Medical Service**

CARSON, H M., M.B Dubl S.M.O Ministry of Health, Go Coast
LOMAZ, JOZEF, M B Polish School of Medicine, Edinbur M O (anæsthetist) Federation of Malaya
READ M. T M.B E. M C, M R.C.S, D T M.&H administra M O (grade A) Federation of Malaya
RUSSELL, H B L, M R C.S, D T.M.&H, D P H S.M.O., minis of health Gold Coast

## Births, Marriages, and Deaths

### BIRTHS

CAMPBELL.—On Feb 6 at St Brenda's Nursing Home B to Mary (née Clarke) wife of Dr A. M G Camp daughter

### DEATHS

HORTON—On Jan. 23, at 119 Queen's Park Avenue, Bourne Robert Lister Horton M.S Lond. F.R.C.S, J.P, aged 65.

# Notes and News

## WORLD HEALTH ORGANISATION

Executive Board of W.H.O at its meeting in Geneva lined its proposed *programme of work for the period* ) The aims are to secure the participation and coöpera all countries and territories to stimulate research and hange of knowledge in health science generally to overnments in developing their health services and note coöperation between neighbouring countries and rith common problems. Under this programme all s will be *encouraged in long term national health g;* the professional and technical education of l health personnel is to be fostered and in countries to provide full professional services W.H.O will assist ing "subprofessional" workers and medical ancillaries. board, expressing concern over reports that malaria mosquitoes are developing resistance to dicophane *resolved to ask the World Health Assembly* to urge nents to intensify their plans for *malaria control.* submitted to the board revealed that over 300 million in the free world are still unprotected against malaria. ard recommended that total malaria eradication should malaria control, even though this would involve a ary *increase* in expenditure

## INTERLINGUA

INNING with the January issue *Circulation* is including ries of articles in Interlingua. In the U.S.A. altogether entific publications, including *Blood* now use Inter as a *secondary language;* and two *further publications* in Interlingua exclusively *This language is composed* ents common to Spanish, Portuguese French, Italian er Romance languages.

## A NEW CHILDREN S WARD

DREN are on the whole keeping fitter than they used with the result that children's *hospitals and even* n s wards are becoming scarcer But at the Hospital John and St. Elizabeth, in St John s Wood London ters of Mercy believe that a hospital without a children s *not* complete. They had one before the war but when ildren were evacuated, the ward had to be turned to rgent uses, and it was not *possible to revive* the old the hard times that followed But now a new ward ly built for the purpose was being opened on Feb 9 Cardinal Archbishop of Westminster St John s and abeth s is a voluntary hospital so the money for this has had to be collected; and contributions have ranged 3500 from King Edward s *Hospital Fund* for London rthing collection from the children of the *neighbourhood.* cost £27 000—nearly half what the entire new buildings 1898 when the hospital moved to its present site from Ormond Street. Only £5000 more remains to be

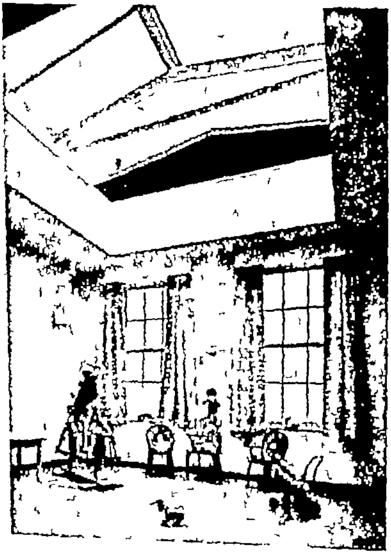
new ward has been built *on* the top of one of the wings old building with its floor mounted *on* a steel frame s flat roof made of corrugated aluminium for *lightness* ouble-hung sash windows let in plenty of light, and allow manent ventilation without draughts. The ceilings spended and the floors are of Spanish cork tiling warm and pleasant to look at.

main ward consists of two four bedded bays the cots so arranged that the occupants can fling remarks to other but not droplet infections The sick child as ames Spence used to remind us, looks up at a ceiling h often seems terribly far off and frightening; but here ceilings are of reasonable height and painted a colour ulingly called buttercup yellow though in fact a particularly winning deep primrose. White or soft blue walls set off this colour and curtains of charming ern rest the eye The ceilings are set with lamps in gracious d shades, and even the screens, curtained in a faint n red, add unobtrusively to the clever subdued colour me At night lights set low in the wall behind small ed grilles send a different light downwards to the floor ing the way for nurses but never dazzling a patient s The cots are made with bars too close together for even smallest inquisitive head to poke through; but the cot are still as heavy as they have always been for nurses ove When are equipment designers going to produce bour-saving cot? Mattresses either interior-sprung or alopillo, are enclosed in waterproof plastic cases. Six cots have poles to carry transfusion fittings, and bed trays with open corners for easy cleaning, hang from the cot sides.

An infants ward, with canvas cots, is warmed by electric panels *in the ceiling which maintain it at a constant convenient* heat in any weather Elsewhere the unit is warmed by plentiful radiators running beneath the windows and round the walls There is a two bed isolation ward with a large glass observation window, and a glass screen separating the beds It has its own water-closet and wash basin, and is also fitted with a cupboard opening both into the corridor and into the ward through which food or necessary equipment can be passed without need *for the person outside to enter the ward.* Two small wards contain single beds big enough to take a grown up person. These will be useful when a mother and baby are admitted together

The treatment room is of the most modern pattern with a refrigerator for blood a telescopic lamp on an adjustable arm a sink and slabs for plaster making and a special ventilating plant which can be switched on to remove sterilising vapours. It will also *serve as a recovery room* for children coming round from anæsthetics Equipment is of stainless steel wherever possible and all appropriate surfaces are covered with Warerite Two sluice rooms are fitted with mechanical bed pan washers The kitchen contains a large refrigerator and a small electric cooker Food is to be brought *to the* ward in an electrically heated trolley which is so slung on its chassis that it travels up and down ramps without ever deviating from the horizontal—a *great safeguard against* the slopping of soups. The doctor s room has an X *ray viewing* panel, a cabinet for records, and a handsome scale for weighing the patients like the rest of the unit it also has a friendly and welcoming air

The *most* unusual room in the unit is the playroom. It is *empty, as a playroom* should be except for toys and thanks to hot water panels set high in the walls it is warm. Moreover it has a splendid outlook over the *hospital gardens* and its windows are so arranged that nobody can fall *out of* them. Its distinctive feature however is the roof: this is of glass and movable Press a button and the roof steadily and soberly slides off out of sight leaving the whole playroom *open to the sky* press another button and back it comes with engaging *precision.* The sisters consider that in this way they have solved the problem of providing both an indoor playroom and an outdoor playground, *both at* treetop level.



Sydney W. Newbery

The playroom with sliding roof.

## NEW RULES FOR MIDWIVES

The Minister of Health has now authorised the use by midwives of trichloroethylene[1], and the Central Midwives Board has approved the following apparatus for its administration

1 Tecota Mark 6 (made by Cyprane Ltd, Haworth Keighley, Yorks)

2 Emotril Trichloroethylene Automatic Inhaler (made by the Medical and Industrial Equipment Ltd, 12, New Cavendish Street London, W 1)

The board stipulates that the apparatus shall be used by a midwife on her own responsibility only if it has been inspected and approved by the board within the previous six months The apparatus must be inspected periodically by the manufacturers, who will arrange with the board for the issue of the requisite certificates Before employing the apparatus each midwife must satisfy the board that she is thoroughly proficient in its use

The new rules provide that midwives shall from time to time attend refresher courses approved by the board

## LABORATORY SERVICE IN EMERGENCIES

The Ministry of Health suggests that throughout the country the services of a hospital pathological laboratory should be available in emergency, both to hospital medical staff and to general practitioners, at times when laboratories are normally closed In some places, according to the Ministry, the arrangements for emergency service are inadequate, whereas in others an undue burden is being placed on laboratory staffs A memorandum to hospital authorities[2] defines two types of emergency service (1) guaranteed, and (2) contingent (i e, the hospital will do its best to carry out the test provided that it can reach the pathologist or technician concerned) For the guaranteed service hospitals should, wherever possible, be grouped together, each taking it in turn to provide this service Hospital authorities are asked to prevent unnecessary use of the emergency organisation, which should not be more elaborate than is required to meet likely demands

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## Royal College of Physicians of Edinburgh

At a meeting of the college held on Feb 1, with Dr L S P Davidson, the president, in the chair, the following were elected to the membership

G J Summers A Muir, D P Puri L E Wynter, S Bell A K Black, M B Morris J A Kay, I M Cuthill, D C Peiris T S Kalyanam, P S Macfarlane H M P Perera, F V Edrisinghe D M Chakraborty, V Srinivasan P M Hewlett G F Trobridge B Kaplan E D Myers M S Karve H S Wong, T A Cunningham, D C Sen F O Simpson C G Caro

## Chadwick Lecture

On Monday, Feb 14, at 5 30 P M, at the Royal Institution of Great Britain, 21, Albemarle Street, London W 1, Sir Hugh Beaver, M INST C E, will give a lecture on Clean Air

## London County Council

The council has agreed to increases in the salaries of its chief officers which will cost £7500 a year

The salary of the clerk of the council rises from £4700 to £5000, those of the chief engineer the architect, and the education officer from £4200 to £4500 and that of the medical officer of health from £4000 to £4250

## Basingstoke Plastic Centre Medical Society

On Thursday, Feb 17, at 7 30 P M, at Rooksdown House (Park Prewett Hospital), Basingstoke, Hants, Sir Harold Gillies will take the chair at a symposium on Fractures of the Long Bones with Soft-tissue Loss The speakers will include Prof J Trueta, Mr J S Ellis, Mr A J Evans, and Mr E W Peet

## St Mark's Hospital, London

On Jan 29 the medical committee of the hospital gave a dinner in honour of Prof J C Goligher's appointment to the chair of surgery in the University of Leeds and also of his appointment as honorary consulting surgeon to St Mark's Hospital In the course of the dinner his successor, Mr Ian P Todd, was welcomed A toast was also drunk in absentia to Mr J P Lockhart-Mummery, the senior honorary consulting surgeon to the hospital who is now living in Hove and will be celebrating his 80th birthday on Feb 14

# Diary of the Week

FEB 13 TO 19

### Monday, 14th

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's In W C 2
4 P.M Sir Cecil Wakeley Hunter and Surgical (Hunterian oration)

MEDICAL SOCIETY OF LONDON 11, Chandos Street W 1
8 30 P M Dr W G Oakley, Mr S M Cohen Diabetic

### Tuesday, 15th

UNIVERSITY OF LONDON
5 P M. (University College Hospital Medical School, Prof Jan Waldenström (Lund) Clinical Inv Hypergammaglobulinæmia.

BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P M (London School of Hygiene and Tropical Keppel Street W C 1) Prof J N Davidson proteins in Cell Structure

ST MARY'S HOSPITAL MEDICAL SCHOOL, Paddington W 2
5 P M Prof. D E Price Gynæcological Pathology

INSTITUTE OF DERMATOLOGY, St John's Hospital, Lisle W C 2
5 30 P M Dr H J Wallace Bullous Eruptions

SOUTH WEST LONDON MEDICAL SOCIETY
8 30 P.M (Bolingbroke Hospital Wandsworth Common, Prof Alan Moncrieff Marasmus

MANCHESTER MEDICAL SOCIETY
4 30 P M (Medical School) Dr G E Smith Medical of Dr Johnson (University lecture)

### Wednesday, 16th

ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street W 1
8 15 P M *General Practice, Dermatology* Dr Ray Industrial and Domestic Dermatoses Dr Be Teaching of Dermatology for General Practice

INSTITUTE OF DERMATOLOGY
5 30 P M Dr Henry Haber Clefts, Vesicles, and Bullæ

EUGENICS SOCIETY
5 30 P M (Burlington House Piccadilly W 1) Mrs Hubback Fertility of Educated Women

### Thursday, 17th

ROYAL COLLEGE OF PHYSICIANS OF LONDON, Pall Mall East, S
5 P M Prof W Melville Arnott Order and Disorder in monary Function (First Oliver Sharpey lecture)

BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P M (London School of Hygiene and Tropical Med Prof J H Gaddum F R.S Effects of Alcohol

ROYAL ARMY MEDICAL COLLEGE, Millbank, S W.1
5 P M Dr W H Bradley Man and Virus

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE, M House, 26 Portland Place W 1
7 30 P M Colonel H W Mulligan Trypanosomiasis in West Africa

INSTITUTE OF DERMATOLOGY
5 30 P.M Dr R W Riddell Diagnosis of Fungous Infecti

BRITISH INSTITUTE OF RADIOLOGY 32, Welbeck Street W 1
8 P M Dr A Robinson Thomas Technique of Sial Mr R T Payne Experiences of Sialography

MANCHESTER MEDICAL SOCIETY
8 P M *Anæsthetics* (Medical School) Dr T H Cha Anæsthesia for Prostatic Surgery

UNIVERSITY OF ST ANDREWS Medical School, Small's Wynd D
5 P M Mr Andrew Logan Benign Ulceration of the Œso

### Friday, 18th

POSTGRADUATE MEDICAL SCHOOL OF LONDON, Ducane Road, W
2 P M Mr D M. Wallace Natural History of Bladder Tu
4 P.M Prof C H Stuart Harris Virus Diseases o Respiratory Tract

UNIVERSITY COLLEGE, Gower Street W C 1
5 30 P.M Prof F Bergel D SC Attempts at Chemothera Malignant Diseases

ROYAL SOCIETY OF MEDICINE
8 15 P M *Radiology* Mr F P Raper Bilateral Symm Peri ureteric Fibrosis Dr P G Keates An Asse of Sodium Acetrizoate and an Experimental Basis for Use in Intravenous Pyelography

FACULTY OF RADIOLOGISTS, 45 Lincoln's Inn Fields W C 2
5 P M *Radiodiagnosis* Dr David Sutton Thoracic A graphy by Percutaneous Transcarotid Catheterisa Dr Conway Don Intravenous Cholangiography a Cholecystectomy

INSTITUTE OF NEUROLOGY
5 P M (National Hospital Queen Square W C 1) Prof G Romanes Motor Cells of the Spinal Cord

OSLER CLUB
7 45 P M (11 Chandos Street W 1) Dr A W Spen James Paterson Ross History of Acromegaly

ROYAL MEDICAL SOCIETY 7 Melbourne Place Edinburgh, 1
8 P M Prof J Chassar Moir Confinements of Some Eng Queens and their Effects on History

ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLAS 242 St Vincent Street Glasgow
5 P.M Mr Iain McLennan Surgical Aspects of Thyroid D

### Saturday, 19th

BIOCHEMICAL SOCIETY
11 A M. (London School of Hygiene and Tropical Medic Symposium on the Biochemistry of Vitamin B

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[1] The Midwives Rules Approval Instrument 1955 S I 1955, no 120

[2] H.M (55)14

# THE FUNCTIONAL SYMPTOMS OF ORGANIC DISEASE OF THE BRAIN

E A. BLAKE PRITCHARD
M.A. M.D Camb., F.R C.P
ICIAN TO UNIVERSITY COLLEGE HOSPITAL AND THE
IONAL HOSPITALS FOR NERVOUS DISEASES LONDON

symptoms of some patients can confidently be reted as due to physical changes in some recognised of the body In many such cases the nature and use of these changes can be reliably discovered— e patient s disease can be fully diagnosed Happily ate of affairs is increasingly common

symptoms of other patients, however patiently y listen to their description and however searching e our inquiry do not arouse in us the belief that are due to derangement of any particular bodily or organs After full consideration of the com , and after exhaustive clinical examination, we e in one of two states of mind

Ve may still be completely uncertain about the t's condition. No bell has been rung no echo of a cantly similar complaint has been aroused, and no iable reaction has been elicited

Ve may have found the patient behaving in a highly cant way, reminiscent of similar reactions and r complaints in other patients. From this we conclude that his symptoms are of a specific form (according to our personal verbal habit) we call onal or hysterical, and which we attribute to some portion between the emotional stress to which he een subjected and his ability to adapt or adjust lf to such disturbances.

s article is not concerned with psychiatric diagnosis oncerned only with the approach to such matters of neral clinician domestic practitioner or consultant ian or surgeon

### Use of 'Functional and 'Hysterical"

first point I want to emphasise is that the use of erms functional and 'hysterical" involves a ve diagnosis They should be applied to a given tom or syndrome only when it has those charac ics which are unhesitatingly recognised as repeated patient to patient in substantially the same form wrong to use them as indicating merely that atures of organic disease have been found or se the patient appears to have an unstable nervous ition If the essential positive characteristics of ctional or hysterical disturbance are absent judg should be suspended further observations made and er help sought Meanwhile our ignorance of what is g with our patient should not be obscured by the of valuable terms which are dangerously misleading they are not applied with precision

recognise a given behaviour pattern as functional sterical is never simple but it is much more complex the patient also presents symptoms of organic se. In all neurological clinics patients are observed have what is described as a ' hysterical overlay ' ome "underlying' and usually chronic organic se Many patients with symptoms due to the ical changes caused by a physical injury also have r symptoms due to a general emotional disturbance to the complications introduced by a claim for pensation

he difficulty is especially great when the organic ges involve the cerebral hemispheres One reason this is that such cerebral damage commonly gives to general disorders of personality of which the ional or hysterical symptoms are merely one es ion. A second reason is that a destructive lesion rtain parts of the brain may render the patient erratic in his performance, extremely variable in his powers of concentration and of attention, and liable to react not only to the content of the special clinical tests applied but also to the circumstances in which the tests are made and to the personality of the examiner This is perhaps particularly true, as Gooddy and Reinhold (1952) have pointed out, of lesions of the parietal lobe

In coping with emotional stress a patient may fail, and present functional or hysterical symptoms either because his personality is abnormally unstable or unadaptable or because the stress is exceptionally severe The instability of his personality may be constitutional or it may arise from structural damage of the brain; but in either case the effect will be the same Hence the functional or hysterical symptoms found in patients with organic disease of the brain may take precisely the same form as those found in psychoneurotic patients who have no structural changes in the nervous system. This may lead to serious mistakes The patient with slowly progressive disease of the brain may be regarded as suffering from a psychoneurosis, and the appropriate investigations may be neglected In the cases described below—all of them recently observed—behaviour regarded as "hysterical ' was the first indication of a cerebral tumour, and was the cause of delay in diagnosis.

The second point to which I want to draw attention is that, in these cases, error might have been avoided if the symptoms had been called functional (using the word in its purely descriptive sense) instead of hysterical (a term which expresses *an opinion* on the cause of the disturbance)

### Case reports

**Case 1**—A married childless woman aged 45 was sent by her doctor for consultation with a complaint of headache continuous since an accidental fall in her home two weeks earlier Although no abnormal physical signs of intracranial damage were discovered she was admitted to University College Hospital for investigation.

An X ray film of her skull was normal, her cerebrospinal fluid (C.S F ) was under normal pressure and normal in composition apart from a slightly raised protein content (70 mg per 100 ml.)

Meanwhile in the hospital ward she had developed fresh symptoms: she claimed that she could not stand and, when asked to do so she staggered about wildly without actually falling and then sat upon her bed saying that her legs would not carry her; she said she was nauseated and made at all times of the day frequent loud retching noises over a vomit bowl without ever vomiting Re-examination on several occasions revealed no signs of structural damage of the brain and these behaviour disturbances were regarded as hysterical.

Discussion with her husband elicited the information that two domestic matters were causing her grave concern. He said that he could take immediate effective steps to deal with these and asked that she might be allowed to return home She was discharged from hospital a week later with the diagnosis of an anxiety neurosis with hysterical features Until that time the only observation which was regarded as suggesting that she might have a structural change in her nervous system was the increase of protein in the C.S.F

A week later her general practitioner reported that her condition was unchanged, that he had engaged a nurse to look after her at home and that this nurse reported that her impression was that the patient was not physically ill but was simulating a state of invalidism; she chatted cheerfully when she was indulged but complained and pretended to feel sick when the nurse wished to leave her A week after this the nurse who had left her a short while before apparently no worse discovered her lying dead in a deck-chair in her garden

*Necropsy* revealed a large infiltrating tumour in the left lobe of the cerebellum.

**Case 2**—Mrs. A a hospital nurse aged 51, with a strong family history of migraine had herself suffered from migraine since adolescence After the menopause at the age of 48 her attacks were of precisely similar form but more frequent She was admitted to the Hackney Hospital because she had

had what was regarded as an exceptionally severe attack, the headache and vomiting having then lasted for three days.

Clinical examination revealed no papillœdema, and no signs of any disturbance of her cerebral activities. Her blood-pressure was 190/130 mm. Hg, and her heart was considerably enlarged. After treatment with ergotamine tablets her headache almost disappeared and the vomiting ceased. Because she seemed depressed she was examined by the consultant psychiatrist, who diagnosed a chronic anxiety state, for which he found ample cause in her personal background.

Ten days after admission she became unsteady on her feet and complained of lack of proper control of the movements of her left arm. Re-examination revealed no abnormal physical signs other than an equivocal plantar response on one side. Because of her unsteadiness she was referred again to the psychiatrist, who reported that this symptom was certainly "hysterical." However, next day examination showed gross nystagmus, spastic quadriplegia, and a definite extensor plantar reflex; there was still no papillœdema. She died two weeks later.

*At necropsy* the left lobe of the cerebellum was found to be entirely destroyed by a necrotic growth, which was not identified histologically.

Case 3.—Mrs. B., aged 50, was referred to the Maida Vale Hospital on June 9, 1953. At the age of 30 she had been investigated and treated for migraine at St. Charles' Hospital.

At the Maida Vale Hospital she was seen when suffering from an attack and vomited during examination. No abnormal physical signs were made out. Radiography of her skull was normal. She was treated with ergotamine tablets and reported six weeks later that she was better.

Two months later she was examined at the Paddington Hospital because she had been for some time in a "hysterical and moderately agitated condition" and had also become drowsy. She was described, when examined, as being "extremely hysterical"; but the presence of "some organic reaction factor" was suspected, although there were no physical signs of any structural damage of her brain. A month later she had a left hemiparesis and she was transferred to the Atkinson Morley Hospital, where ventriculography revealed a deep thalamic mass on the right side. She died a month later.

*Necropsy* disclosed an astrocytic glioma of group II.

Case 4.—A man, aged 65, married but separated from his wife, had been a very successful surveyor. He was examined in his home at the request of his private doctor because he had abruptly lost his memory.

For the previous twenty years he had had very infrequent attacks of transitory mental confusion but no clear loss of consciousness. On two of the occasions (three and two years before his examination) he had had brief weakness of one limb. When he was first examined he gave no indication of recognising either his wife or his doctor; he was apparently completely without knowledge of the hour, day, month, or year, and he could not give his address. Nevertheless he discussed, without hesitation, details of the concerns and practice of a surveyor, and he manipulated figures with astonishing rapidity and accuracy. Physical examination revealed no motor, reflex, or sensory signs of localised disturbance of his brain. He was admitted to University College Hospital in February, 1951.

X-ray photographs of his skull were normal. His blood-pressure was 160/90 mm. Hg, and his retinal vessels and optic discs were healthy. He seemed completely disoriented in time; he called the hospital a "curative institution" and the nurse a "female attendant." A psychiatrist reported that his amnesia was "hysterical" and appeared to be lessening. However, the C.S.F., though under normal pressure, contained 120 mg. of protein per 100 ml. An air encephalogram was normal. The psychiatrist re-examined him and reported "I think now that he is not really unable to remember and is determined to forget." His mathematical ability was still extremely good; he multiplied 35 by 46 correctly before the examiner had time to write down these numbers. Special tests of parietal-lobe activity were made and reported on as indicating a left temporoparietal tumour and possibly a lesion of the right parietal cortex. A ventriculogram revealed a normal and symmetrically placed ventricular system. The patient gradually became quadriplegic and drowsy.

*Necropsy* six months after his original admission to hospital revealed a tumour of the corpus callosum.

## Discussion

These protocols illustrate the fact that organ disease may give rise to symptoms of the kind com called hysterical, and that these symptoms may b first manifestation of such disease. They th illustrate the danger of describing any disturb behaviour as hysterical until its psychoneurotic b been firmly established. This word "hysterical" always connotes a disturbance originating in psy *logical abnormalities*. Thus Henderson and Gi (1940) say that it

> "has come to be associated also in psychopathological fi with the operation of a particular kind of mental pr The 'hysterical reaction' shown by the 'hysterical pe ality,' although in the majority of cases mixed with types of psychopathological reaction, e.g., with contributes to the total picture symptoms which are d tive both clinically and psychopathologically. Fin manifestations of hysteria include motor symptoms su paralysis, contracture, involuntary movements, mut aphonia and sensory symptoms, including anæ paræsthesias, hyperæsthesias and hysterical fits."

The responsibility for deciding that a given sym is not a sign of organic damage is that of the phys or surgeon in whose department the patient appea advice. Thus the decision that cardiac palpitation precordial discomfort are not due to dyspepsia cardiac disease can only reliably be made by the ge physician or by the cardiologist; the decision "fainting turns" or "blackouts" are not due to epi or to syncope is only reliably made by the neurol the decision that pruritus is not due to *local inflamm* is only reliably made by the dermatologist; and But when this decision has been made on the nat a given symptom, it is the psychiatrist's task to elu its *cause* and to prescribe for its relief. He al competent to decide whether the psychological ba hysteria is or is not present in a given case, an term "hysterical" must no longer be applied o merely negative ground that no organic disease has found.

The term "functional," on the other hand, do more than describe a particular kind of beha disturbance, and is applicable when we do not whether the cause is in the mind or in the brain or in

### *Functional Nervous Disturbances*

*I must admit that in the most* recent textboo neurology and of psychiatry no use is made in this of "functional," which has fallen into disrepute.

Though the term was frequently used earlier, I found no definition of "functional nervous disturb before the time of Gowers, who wrote of four varie disturbance—organic, structural, nutritional, and tional (Gowers 1886). An organic disease wa accompanied by a macroscopic lesion of the ne system. Structural diseases were those whose could be detected only by microscopy. Nutri diseases and functional diseases (Gowers *said*) coul always be sharply distinguished from one an because nutrition and function were mutually depen and because long-continued functional disturbance determine nutritional changes. If certain grou neurones were active for long, metabolism migh altered, and thus functional disease might be nutritional. It is clear that by the function of a of neurones Gowers meant simply those of their acti which had been demonstrated by biochemical electrical stimulation, and destruction paralysis—to we could now add *electro encephalography*.

This concept of functional disease, as due only t disturbance of activity of neurones without ph change, did not survive the rapid development of n physiology which followed Gowers. Soon afterwa ted out that cerebral tumours, arterial infarcts, r gross lesions of the brain do not produce ymptoms per se, but do so only in terms of, and xtent of their interference with the normal *of the nervous tissue which has been damaged* en claimed that all organic lesions are functional manifestations, since the functions of neurones r activities were regarded merely as different referring to the same thing The term *func-* eased on this basis to have any valid significance into disuse

*nd Function*

the reason why 'functional ' did not survive ense and useful term was that the notion of was uncritically equated with that of activity ne assumption that they provide different ways ing to the same thing has been responsible for f the confusion of thought over the relation structure and function in the human cerebral It is too often believed that, when activity has served function has been manifest it is even that, when a given part of the brain is destroyed lting disturbance of behaviour enables us to ot only what were the effects of its normal activity o what are its normal functions This same n is referred to by Le Gros Clark (1952)

> eems possible indeed that there may have been a rstanding of the term function as it has been used ent writers in some of the recent discussions on cortical ion."

immediate aim of neurophysiology is to define o regularly occurring series of activities in nervous res which can be related causally Thus when it d that activity in the rolandic motor cortex is d in sequence by activity in the corticospinal y by an alteration in activity of the segmental atter of the spinal cord, by activity in the anterior ells and in the emergent anterior spinal roots, and by contraction of the muscles to which these are uted we have grounds for thinking that we have red a normal physiological process and not merely andom effect of experiment

en such a causally linked series of activities is d as a whole, it is permissible to add to this notion se (in the operative sense) that of purpose (in the gical sense) Thus we may postulate that it is a pose of activity in ' or function of ' the cortico neurones to achieve this particular alteration in the ty of the segmental spinal grey matter and lower r neurones and we may suggest that this is why structures are 'organised in that manner it is important to note that only the *activities* of nervous structures can be observed and demons d; their *functions* although they may be inferred may be asserted can be neither observed nor onstrated.

at the correct use of the word function ' neces y involves this teleological notion of purpose as osed to the mechanistic notion of causation is to be from one of the *Shorter English Dictionary* definitions unction as the special kind of activity proper to hing; the mode of action by which it fulfills its pose In many nervous structures we observe vity and yet have at present no adequate conception its significance for us such structures have definite vities but no recognised functions The converse— the assertion that a given structure has a certain tion although it has no demonstrated activity— lates an essential principle of scientific discipline

*ctional Basis of Hysterical Symptoms*

There are many forms of motor paralysis, of sensory , of involuntary movement and of personality disorder involving amnesia for which the term ' functional " in the *above mentioned* sense, is peculiarly appropriate though they are commonly called hysterical —e.g , by Henderson and Gillespie (1940)

Thus, where there is "hysterical weakness ' of an arm we find that every movement which the patient is asked to make although it may be produced with a facial grimace and a general bodily contortion indicating great effort has its effectiveness reduced *to a minimum* A hand grasp made on request is produced by flexing the fingers and thumb around an object placed in the palm and then fixing them rigidly and often tremulously in a position in which they exert the least possible pressure on the object grasped Further, the amount of pressure so exerted is the same whether the object *grasped* is *comparatively* thick (e g , the examiner's forearm) or whether it is comparatively thin (e g one finger) and the normal movement-synergism of wrist extension is often absent Higher in the arm a given muscle group may be put into strong contraction when the patient is asked to maintain a posture in opposition to a displacing force although it is contracted weakly or not at all when he is asked to produce an active movement for example, the elbow may be strongly fixed in flexion, although almost no contraction takes place in the biceps muscle when flexion from the extended position is asked for

In such a case it is clear that what the patient has lost is not the ability to contract his muscles but the ability to perform movements not the ability to main tain a posture but the ability to alter the position of his arm not the ability to flex his fingers but the ability to grasp In fact, what has been lost is nothing which *can be ascribed to loss of normal muscular or neuronal* activities but something which can only be described in terms of " use of the limb that is to say, the loss is strictly " functional in the proper sense of that word for it is the loss of that behaviour of his limb which has significance to the patient Experience shows that, just as the alternative picture of spastic paresis of the arm due to cortical damage can be reliably ascribed to loss of activity in various corticospinal neurones, so also the " hysterical ' form of paresis cannot be ascribed to structural damage at any level of the nervous system and *can be comprehended only in terms of loss of* " use of the arm

Similarly an area of " hysterical " anæsthesia has a distribution which cannot be explained in terms of any neuronal damage, peripheral or central Moreover this area may become insensitive only so far as this loss is believed by the patient to be of significance: thus in many cases of hysterical anæsthesia response to pinprick is completely lost, yet responses to other forms of stimulus are preserved or only slightly impaired It is an area which corresponds to the patient s concept of what constitutes a distinct and separate part of his body the patient has lost his ability to respond, in a way which is of significance to him to stimuli applied to an area of his body which is ' represented in his mind " and not in his brain Hysterical blindness of one eye and hysterical deafness of one ear are further examples of a form of insensitivity which corresponds to the significance which the patient attaches to a particular variety of disability; the pupillary contraction to light and all other photic responses to illumination that can be separately assessed are intact and only the use of the eye for seeing ' —i e the ' function *of* the eye—is lost

## Summary

The symptoms commonly known as *hysterical* palsies anæsthesias contractures and fugues occur sufficiently often, and in sufficiently stereotyped form, to be reliably identified in the neurological clinic

These symptoms may arise in a patient who has no organic disease, and in such cases psychiatric investigation may show that they are due to a psychopathic instability which is intrinsic and constitutional Then—but not until then—the term "hysterical" can properly be applied to them

But precisely similar symptoms may be an early manifestation of an organic disease of the brain, and until this possibility has been excluded, and a psychiatric diagnosis has been made, all such symptoms should be described as "functional"—a purely descriptive term *conveying no opinion as to causation*

To apply the word "hysterical" to symptoms which may in fact be due to organic disease of the brain will sometimes delay proper investigation and treatment and thus be a serious error

In this context the word "functional" is not a neologism invented to meet a special requirement which perhaps arises from our present lack of knowledge it is a term of repute which merely needs greater precision in its application As here applied it emphasises the element of *purpose* which is inherent both in its etymology and in the character of the symptoms to which it is attached These *symptoms can be comprehended only* in terms of their significance to the patient, and this significance is purposive in its implications

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# RECURRENT GENITAL AND ORAL ULCERATION WITH ASSOCIATED EYE LESIONS

## BEHÇET'S SYNDROME

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THE "triple syndrome complex" of recurrent genital *and oral ulceration associated with lesions of the anterior* chamber of the eye was described by Planner and Remenovsky (1922) Behçet (1937, 1938, 1939, 1940) emphasised that it was a clinical entity It has since been raised to the status of a syndrome, to which Behçet's name has been attached (Jensen 1941, Berlin 1944) From time to time cases have been recorded, mainly from the Mediterranean area

Curth (1946), reviewing 19 published cases, first suggested that the diagnosis should be applied when two of the three main features were present Certain other lesions have been observed in association with the triad —notably skin lesions resembling erythema nodosum and erythema multiforme, monarticular arthritis, various central nervous manifestations, and thrombophlebitic episodes

Behçet's syndrome has seldom been recorded in this country Whitwell (1934) described recurrent buccal and vulval ulcers associated with embolic phemonena in skin and eye, which are the clinical manifestations of the syndrome, Thomas (1947) published 1 case, and we briefly described 7 (Phillips and Scott 1954) These 7 and 3 additional cases are now discussed in detail, since such patients present considerable difficulty in diagnosis and treatment These 10 cases were observed in the gynæcological clinics of the United Birmingham Hospitals in the last three and a half years At the onset of the symptoms the patients were aged 11 to 48 years, and, when they were first seen their disorders had been present for from five twelve years

TABLE I—ANALYSIS OF SOME FEATURES

| Feature | Case no | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 |
| Age at onset (yr) | 45 | 15 | 35 | 26 | 35 | 28 | 24 | 11 |
| Parity | 3 | 0 | 2 | 0 | 2 | 1 | 0 | 0 |
| Menstrual irregularity | + | | | | + | | | |
| Ulcers related to menses | | + | | | ? + | ? + | + | + |
| Miscellaneous | Carcinoma of larynx | | | | Psychosis | | | |

TABLE II—DISTRIBUTION OF LESIONS

| Site | Case no | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 |
| Vulva | +* | +* | + | +* | + | +* | | |
| Mouth | + | + | +* | + | +* | + | + | +* |
| Eyes | + | | + | | | + | +* | + |
| Joints | | | + | + | | + | + | + |
| Central nervous system | + | | | | | + | | + |
| Skin | | | + | | | + | | + |

* Site of initial lesion

### Clinical Features

#### PRESENTING SYMPTOMS AND COURSE

All the lesions tended to heal and to recur taneously with a variable periodicity Genital, oral eye lesions often occurred at separate times In instances the patient complained of pain at the the lesions, the pain notably preceding the appear of the ulcers by several days and often being of incap tating severity Dyspareunia was associated with genital ulcers Several patients could not eat normal diet, because of the painful oral lesions In

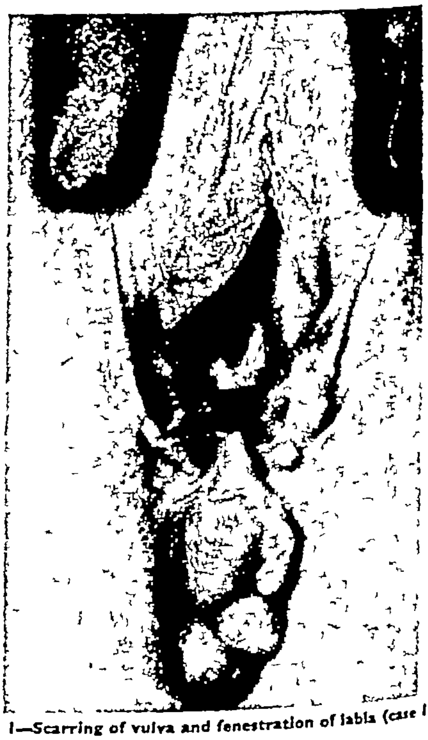


Fig 1—Scarring of vulva and fenestration of labia (case 1)

rteen years elapsed between the initial outbreak l ulcers and the development of eye lesions, the enital lesion having appeared three years before. quent relapses following mild respiratory infections reported by Wien and Perlstein (1932), Mosbley and Curth (1946) This same tendency was t in our cases 1 3, and 6 Behçet reported the of the syndrome after surgical treatment of a nant tumour The lesions in case 1 began after laryngectomy for an epidermoid carcinoma. ressive psychosis was associated with the onset of toms in our cases 6 and 9

these patients were in the reproductive period. In es the menstrual cycles were irregular and the es prolonged; there was no pelvic lesion to account ds. 5 of our patients (see table I) showed a menstrual onship but, though the lesions in some cases d to appear or become worse in the premenstrual e no definite conclusion could be drawn about the

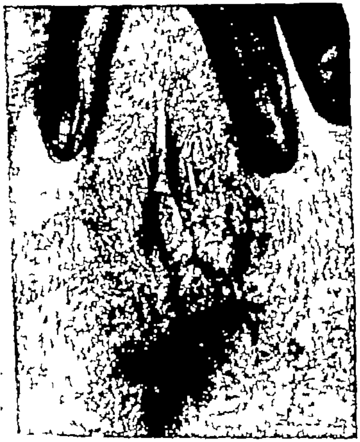


Fig. 2—Ulceration of vulva (case 6)

e of the menses. This is in agreement with Curth's 46) previous observation.

LESIONS

The distribution of the lesions and associated factors shown in tables I and II

*nital Ulcers* (figs 1 and 2)

All the patients except case 7 complained of vulval ers which were 0·5–5 0 cm in diameter and mainly nfined to the vulva, although a few occurred in the oin, on the perineum on the vaginal walls and in cases as high up as the cervix Excavation was a riking feature of the ulcers, and in 2 cases there was estration of the labia minora; in others the whole ulva was progressively destroyed by successive out reaks. Healing when it took place was associated with considerable scarring further deforming the vulva. esions in the vagina or on the cervix were often asso iated with a profuse purulent discharge, from which owever no characteristic organisms could be cultured.

*ral Lesions* (figs. 3 and 4)

The oral lesions were similar to the genital ulcers but tended to be smaller Commonly they were sited on the lips near the mucocutaneous junction on the tongue and on the buccal surface of the cheek; in 3 cases they were found on the palate. 2 patients stated that they

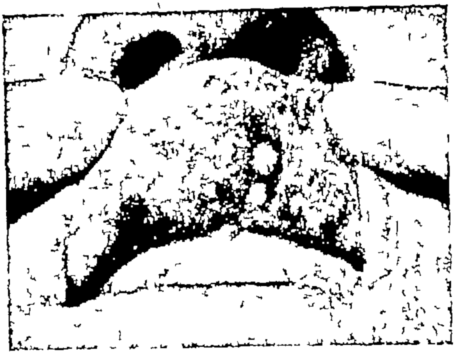


Fig 3—Ulceration of upper lip (case 9)

had previously had painful lesions in the region of the tonsils and in the œsophagus

*Eye Lesions*

The eye lesions usually began as bouts of superficial inflammation each subsequent attack tending to be more severe and proceeding in 3 cases to definite iridocyclitis. In 1 case this process ended in complete blindness.

Case 7 was first seen in March 1954 at the age of 24, her presenting symptoms being intense eye soreness and pain of about seven months duration, but she also complained of oral ulceration of about four months duration Four years previously she had consulted an ophthalmologist because of long-standing eye trouble Examination then showed a right iridocyclitis with corneal dystrophy and a secondary cataract. Shortly after this she was admitted to hospital with left iridocyclitis which responded to conservative treatment. In July 1953, she had an exacerbation of the left iridocyclitis, which responded to cortisone therapy Shortly after this she was married and had a recurrence of the ocular pain and inflammation with each menstrual period. Three months later oral ulcers were first associated with the exacerbation of the ocular symptoms during menstruation.

*Examination* at the time of the menses showed that both eyes were very injected and that she had very little sight in

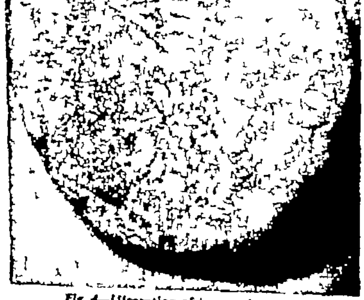


Fig 4—Ulceration of tongue (case 1)

either eye The ophthalmologist reported bilateral cataract and cells in the aqueous consistent with iridocyclitis

*Joint Lesions* (fig 5)

When present the joint lesions were monarticular, and the joint affected in any patient was always the same one The knees, ankles, and wrists were the joints most commonly involved, during an exacerbation there was effusion into the joint associated with limitation of movement and a variable degree of pain After such an episode the joint function returned to normal

*Central Nervous System*

Nervous system symptoms and signs varied from minor episodes of headache and giddiness to major attacks with associated diplopia, blurring of vision, vomiting, and nystagmus

Case 6 was first seen in October, 1953, at the age of 27 She complained of vulval ulcers of ten months' duration and oral ulcers of rather more than twelve months' duration During this time she had had recurrent swelling of her ankles and wrists In April, 1954, she returned with left facial palsy and complained also of blurring of vision, headache, vomiting, and dizziness

*Examination* showed that the right optic disc was very blurred, and that there was some dilatation of the retinal vessels There was also a sustained lateral and vertical nystagmus, the facial palsy was more or less complete and of lower motor neurone type The abdominal reflexes were absent and the plantar responses doubtful, and her gait was ataxic The cerebrospinal fluid showed no abnormality Although the clinical picture resembled disseminated sclerosis, her neurological signs and symptoms were thought to be due to involvement of the nervous system by the same process as was causing her orogenital lesions The attack was transient, but minor recurrences have taken place

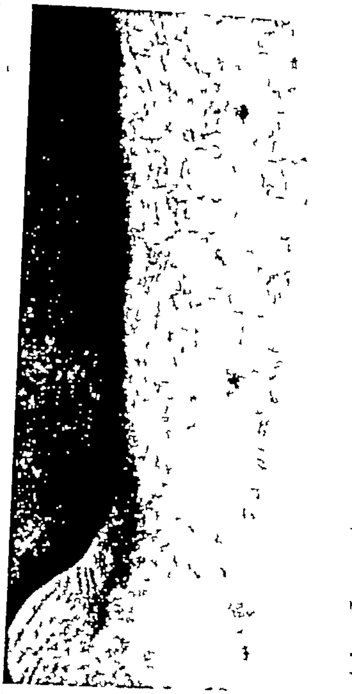
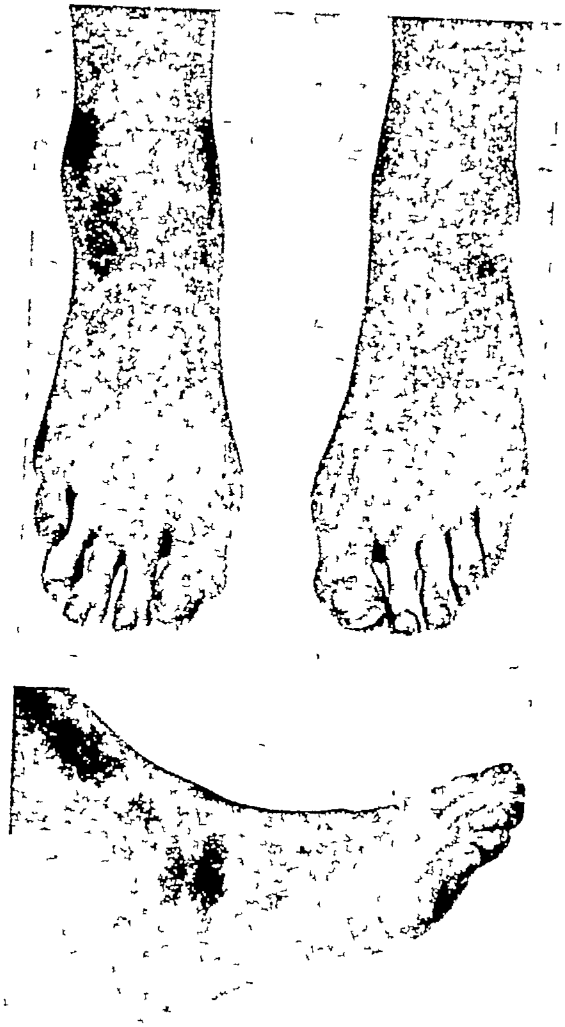


Fig 6—Skin lesion showing nodules erythema nodosum on leg (case 3).



ig 5—Effusion in, and pitting œdema over, right ankle-joint (case 3)

Similar findings had previously been reported in association with Behçet's syndrome (Knapp 1941) Berlin (1944) has also described nervous system signs and sympt Meningo encephalitic episodes were striking featur the 3 cases described by Silfverskiold (1951) and th case reported by Magni (1951)

*Skin Lesions* (fig 6)

The skin lesions tended to be transient and con of nodules resembling erythema nodosum and affe both arms and legs These lesions appeared sometim when there was no exacerbation of the orogenital s and usually lasted less than a week, healing wi leaving residual signs

## Laboratory Investigations

The investigations made were as follows

*Hæmatological* red-cell and white-cell counts, blo erythrocyte sedimentation rate

*Serological* Wassermann reaction Khan test gono complement-fixation test, Frei complement-fixation tes antigen reactions Mantoux test

*Histological* biopsies of oral and vulval ulcers

*Bacteriological* cultures of urine and swabs from lesions

*Cytological* Papanicolau smears

*Endocrinological* estimations of urinary gonadotrophin

*Biochemical* ascorbic acid saturation tests, fractional tes fat-balance, serum-electrolytes

*Radiological* radiographs of chest to exclude tuberculos barium flocculation to exclude abnormality of small gut

None of these investigations showed any notew abnormality, except that in several cases the asco acid saturation test showed reduced levels In ca there was a complete deficiency, but correction of t with large doses of ascorbic acid had no effect whate on the lesions The patient was then eating very li because the oral lesions were so painful This w presumed to be the cause of the deficiency

*Pathology*

Histological examination of biopsy specimens fr mouth, vulva, and skin showed no distinctive patter The ulcers showed granulation tissue being superseded b round cells The skin lesion showed mild round-ce infiltration around the capillaries and sweat gland d There was no histiocytic proliferation or fibrinoid necros Examination of the vulval biopsy specimen for vi infection in 1 case gave an indefinite result regarding th presence of inclusion bodies o histological findings on biopsy of the oral and al ulcers reported by other workers (Curth 1946, ce et al 1951) are similar to those found by us, in some previous cases thrombophlebitic foci have observed At necropsy in Berlin's (1944) case the tial changes found were predominantly of chronic mmatory nature

e central nervous system showed a chronic inflam ory reaction with multiple areas of softening, mainly lving the substantia nigra The necropsy findings ilfverskiold's (1951) fatal case showed a similar ure of widespread focal infiltrations in the brain and al cord, with large areas of softening localised arily in the peduncles and medulla oblongata but present in the thoracic portion of the spinal cord beyond the focal areas there was perivascular d-cell infiltration The necropsy in Magni's (1951) showed no other abnormalities

## Treatment

lany therapeutic agents have been tried at one time nother on the unfortunate victims of this syndrome. al claims for success were made for œstrogens eley 1941) and anti histamines (Koch 1950) but er workers using œstrogens have reported partial porary or no improvement Probably the cyclical ure of Behçet's syndrome has given a false impression uccess The case of Koch's which responded to an histamine presents features which throw doubt on diagnosis

We have found that the treatment of these patients presented a difficult problem and in view of the dency to spontaneous remission the assessment of response to any specific therapy is even more difficult ny of the remedies used had no beneficial effect icillin streptomycin aureomycin chlorampheni sulphapyridine organic arsenical preparations i histamines high protein and low fat diet and lunderbuss therapy with vitamin A thiamine otinic acid, riboflavine ascorbic acid and vitamin E case 2 œstrogen appeared to control the outbreak no other case showed a similar response Local tments were of little value, but eusol dressings ped to maintain cleanliness and on occasion cauterisa n of exuberant granulations seemed to accelerate aling Often analgesics were necessary for the relief pain

Conflicting reports have appeared about the efficacy cortisone and corticotrophin in Behçet's and related ndromes France et al (1951) Kenet (1951), and rth (1952) have each treated single cases without efinite effect However since cortisone and cortico ophin were known to affect eye lesions identical with hose occurring in Behçet's syndrome and had been eneficial in similar skin lesions, we decided to try heir effect on 4 of the most severely incapacitated atients

**Case 1** who had had oral and vulval ulcers for twenty onths, had a severe exacerbation of ulcers in both sites in April 1954 Therapy was started with oral cortisone acetate 25 mg t.d.s The lesions regressed rapidly and healed within a week This remission persisted; but when an attempt was made in June 1954 to reduce the dosage of cortisone there was a severe recurrence Since the oral ulceration persisted a course of intravenous corticotrophin 25 mg daily for five days was given There was good improvement after the first transfusion, and at the end of this short course the ulcers had completely healed Cortisone therapy 75 mg daily was then re-established since then there has been no further relapse

**Case 3**, who had been under observation and treatment since August 1952 with persistent recurrences of oral and vulval ulcers associated with eye changes and skin and joint lesions, had a severe relapse in October 1953 when she developed large ulcers in her mouth and three ulcers of the vulva A two week course of intramuscular corticotrophin 60 mg daily (total 1080 mg) led to a speedy and complete remission Three months later the lesions returned and were as severe as before; treatment with oral cortisone 50 mg daily was started and has been continued and since this time she has had no further relapse

**Case 6** was first seen in October 1953 with ten months history of vulval ulceration and twelve months history of oral ulcers and joint swelling Ophthalmological examination showed changes consistent with mild iridocyclitis After full investigation a remission occurred but in March 1954 she again attended with several small painful lesions on her mouth and vulva When two weeks later these were still getting bigger treatment with oral cortisone acetate 50 mg daily was started Shortly after this the patient's central nervous system became involved (see above) Cortisone therapy was continued and with rest and physiotherapy her signs and symptoms subsided She remained well until July 1954 when she was again seen with oral and vulval ulceration and signs of nerve involvement Cortisone was stopped and a seven-day course of intravenous corticotrophin 25 mg daily was given which led to healing of the ulcers and clearing of the symptoms and signs of the nervous system Since then the remission has persisted on a maintenance dose of cortisone 75 mg daily

**Case 7** had had iridocyclitis for four years when she was first seen in March 1954 but for the previous seven months eye exacerbations were associated with menstruation and she had also had episodes of oral ulceration Treatment with oral cortisone acetate 50 mg daily was started shortly after an acute bout At the time of her next menstrual period she had a less severe attack The dosage was increased to 200 mg daily during the following menstrual period and no outbreak occurred. This régime has been repeated for six successive menstrual periods without a relapse

In the light of our experience in the present series it is doubtful if the dosage used in some of the published cases was adequate or the treatment continued long enough We consider that the response of these 4 patients is both satisfactory and encouraging

## Discussion

Whitwell (1934) aptly remarked that the study of published cases reveals many names but little enlighten ment and this is largely true today Neumann (1895) first described the association of genital and oral ulcers Lipschutz (1923) discussing ulcus vulvæ acutum (Lip schutz ulcers) noted the occasional association with similar lesions in the mouth As stated previously the first observation of eye lesions with genito-oral ulceration was made by Planner and Remenovsky (1922)

Behçet (1937 1938 1939, 1940) established the triad as a disease sui generis Confusion, however, tended to persist through the use of multiple terminology Curth (1946) and France et al (1951) did much to clarify the position France et al reviewed 31 cases of the full triad and described 1 additional case Curth (1946), Whitwell (1934) and Adamantiadis (1951) have empha sised the length of time which may elapse between the appearance of the initial symptoms and the development of the full triad We have adopted Curth's suggestion of applying the diagnosis to cases showing *two* of the three main features, and cases showing one feature have been watched for the appearance of others

A serious aspect of the syndrome is the occasional occurrence of signs and symptoms indicating involvement of the central nervous system. These have been recorded by Behçet (1937 1938 1939 1940), Knapp (1941) Berlin (1944) Thomas (1947) Gray (1950) Silfverskiold (1951) and Magni (1951); and Ashby and Lazar (1951) noted similar occurrences in the Stevens Johnson syn drome These manifestations may resemble those of disseminated sclerosis (as in case 6), whereas focal signs associated with severe headaches may suggest intra cranial neoplasm. In other cases headaches and vertigo were the only symptoms. In 4 fatal cases (Berlin 1944

TABLE I—SUMMARY OF CASES OF BENIGN ESSENTIAL HYPERTENSION TREATED FOR MORE THAN THREE

| Case no | Sex | Age (yr ) | Main clinical features | Duration of treatment (weeks) | Average blood pressure before treatment (mm Hg) | Average fall in blood pressure (systolic/diastolic) (mm Hg) | Result |
|---|---|---|---|---|---|---|---|
| 1 | M | 59 | Left ventricular failure angina, intermittent claudication | 16 | 205/110 | 20/15 | Treatment discontinued owing to cerebral thrombosis |
| 3 | M | 49 | Left ventricular failure and œdema | 68 | 180/130 | 5/15 | Full time work until death from dis- aneurysm of aorta |
| 4 | M | 53 | Left ventricular failure, ? myocardial infarction | 83 | 210/125 | 30/10 | Full time work, no left ventricular failure |
| 10 | M | 50 | Left ventricular failure hypertensive encephalopathy | 45 | 225/125 | 35/10 | Full time light work until death from hæmorrhage |
| 11 | M | 48 | Severe headaches | 85 | 230/130 | 70/20 | Full time work no further headaches |
| 15 | M | 56 | Left ventricular failure | 80 | 240/135 | 60/20 | Remained incapacitated, death from "methonium lung" |
| 16 | M | 54 | Cerebral Thrombosis | 77 | 255/130 | 65/15 | Full time work |
| 17 | M | 59 | Left ventricular failure | 89 | 245/140 | 65/50 | Full time work, no left ventricular failure |
| 21 | F | 50 | Headaches anxiety state | 50 | 200/130 | 10/5 | Full time work, subjective improvement, headaches |
| 22 | M | 46 | Severe hypertension, mild hemiplegia | 33 | 205/145 | 45/30 | Full time work |

"Average blood pressure before treatment" represents the arithmetical mean of all readings made during the period of hyp with hypertensive symptoms

"Average fall in blood pressure" is derived from the average of all blood pressure readings taken with patient standing and lying beginning and end of each follow up outpatient attendance

he is now a patient in a chronic ward Case 26 was admitted apparently moribund from cerebral œdema He made a good initial recovery and led a restricted life at home until his death from uræmia six months later

Thus, of the 17 patients treated for more than three months 12 returned to full-time work, of whom 3 have since died In addition, 2 other patients derived considerable benefit but did not return to work

### FUNDI

In all the 7 patients with malignant hypertension who were treated for more than three months the papillœdema disappeared, and this improvement was maintained during the period of treatment The patients with benign hypertension all had hypertensive retinitis classified as grade II (Keith et al 1939) except 1 patient classified as grade I There was no change of grading in these patients while under observation

### CONTROL OF BLOOD PRESSURE

The average blood pressures before treatment and the average falls as a result of treatment are given in tables I and II The reading before treatment represents an average of all readings made during the period of hypertension with hypertensive symptoms The average number of measurements before beginning treatment was seven The readings during treatment are der from the measurements at outpatient attendances the period of stabilisation At each attendance readings were taken, with the patient standing and at the beginning and at the end of the interview average number of measurements on each patient fifty These readings were taken at an average inter of 3 9 hours after the last injection of H M B

The blood pressure varies greatly from time to time any one patient, and individual blood pressure figu taken at an outpatient attendance may not give adequate picture of the effectiveness of treatment figures for reduction of blood-pressure represent *minimal* fall over twelve of the twenty four hours, *the average interval after injection* was nearly hours and injections were given three times a d *Moreover the dosage of* H M B is determined by presence of mild hypotensive symptoms rather than individual blood pressure readings, indeed treatment usually adequate only when mild side effects are experienced within an hour of the injection

### OBJECTIVE TESTS OF RENAL AND CARDIAC FUNCT

In 7 cases these tests were repeated after period treatment of ten to twenty months Teleradiograp showed no appreciable change in heart size in any ca

TABLE II—SUMMARY OF ALL CASES OF MALIGNANT HYPERTENSION

| Case no | Sex | Age (yr ) | *Diagnosis* | Main clinical features | Duration of treatment (weeks) | Average B P before treatment (mm Hg) | Average fall in B P (systolic/diastolic) in outpatient (mm. Hg) | Result |
|---|---|---|---|---|---|---|---|---|
| 9 | F | 20 | Essential hypertension | No symptoms | 64 | 250/135 | 90/20 | Full time housework |
| 12 | M | 58 | Essential hypertension | Left ventricular failure failing vision | 50 | 275/170 | 65/45 | Full time work until death from dissecting aneurysm |
| 13 | F | 47 | *Chronic* nephritis | Œdema | 35 | 235/145 | 55/20 | Treatment stopped after general deteri tion death from uræmia 6 mos late |
| 14 | M | 61 | Type II nephritis (Ellis) | Left ventricular failure, œdema | 34 | 280/135 | 60/40 | Initial improvement later disabled œdema and treatment stopped |
| 18 | M | 48 | Essential hypertension | Effort dyspnœa œdema | 61 | 245/135 | 55/30 | *Full time work* |
| 23 | M | 46 | Essential hypertension | Dyspnœa hæmaturia and headaches | 36 | 245/155 | 60/35 | Full time work |
| 26 | M | 59 | Essential hypertension | Moribund cerebral œdema | 2 | 235/150 | 30/40 | Good initial recovery restricted life at h until death from uræmia |
| 10 | F | 46 | Post toxæmia of pregnancy | Effort dyspnœa œdema | 8 | 280/170 | Insufficient data | Sudden death congestive failure (necrop |
| 20 | M | 54 | Essential hypertension | Effort dyspnœa œdema | 7 | 240/150 | Insufficient data | *Died of paralytic ileus and peritonitis* |
| 24 | M | 31 | Type II nephritis | Effort dyspnœa, œdema | 5 | 245/110 | Insufficient data | Death at home (no necropsy) |
| 25 | M | | Essential hypertension | Uræmia | 6 | 225/145 | Insufficient data | Death from uræmia and overdose of hex methonium |

etrocardiography showed no change in 3 patients lerate improvement in 3, and moderate deterioration

The results of blood urea estimations and examina s of the urine are given in table III The urine tests roved in 3 cases deteriorated in 1, and showed no nge in the remaining 3

## Difficulties and Complications

*e-effects*

he incidence of the common side-effects in the whole es is shown in table IV Constipation and postural tness were the most common, and diarrhœa and al disturbances the next most common A few ents had difficulty in micturition The skin reactions prised two allergic rashes and one complaint of sistent pain after injections In addition mild icular sepsis was commonly seen and may have been to mild bromism The side-effects tended to be more ere in the early weeks and later became much less ublesome Side-effects occurred less commonly in ents with malignant hypertension than in those h the benign form and in no case of malignant pertension was treatment discontinued because of e-effects

We have made repeated checks of the serum bromide els and have never found concentrations higher than mg per 100 ml

*eatment Discontinued within Three Months*

In 5 patients with benign hypertension treatment was continued within the first three months One patient ad an allergic reaction with fever, arthritis, and sore hroat This may well have been due to the retard edium and treatment might have been continued with oluble H M B Another patient had severe postural intness and the remaining 3 patients in this group were ound to be temperamentally unsuitable for prolonged reatment In 2 cases the symptoms were mainly those of an anxiety state; the patients had been wrongly elected for treatment and the treatment proved too rigorous for them The 3rd patient was symptom free but had grade III retinopathy she also found the side effects too distressing and stopped treatment but has since developed malignant hypertension

BLE III—CHANGES IN BLOOD UREA LEVELS AND URINE IN PATIENTS TREATED FOR PERIODS OF 10–20 MOS

| ase no. | Interval between tests (mos ) | Blood urea level (mg per 100 ml ) |  | Urine † |
|---|---|---|---|---|
|  |  | Before treatment | After treatment* |  |
| 1 | 20 | 65 (2) | 42 (2) | Improvement |
| 9 | 13 | 38 (3) | 34 (2) | Improvement |
| 11 | 10 | 42 (2) | 40 (1) | No change |
| 16 | 19 | 40 (1) | 37 (2) | No change |
| 17 | 20 | 50 (1) | 56 (1) | Deterioration |
| 18 | 13 | 42 (2) | 40 (1) | No change |
| 23 | 10 | 64 (2) | 44 (1) | Improvement |

Figures in parentheses refer to the number of estimations from which the average figure is derived

Improvement means disappearance of albumin and/or red blood cells and casts, and deterioration means their appearance

*Deaths under Treatment*

9 patients died while under treatment with H M B 6 of these had malignant hypertension Table V summarises these cases 1 patient died as a result of treatment of paralytic ileus (Goldsmith 1955) and another of "methonium lung" (Doniach et al 1954) The latter had developed increasing dyspnœa and radiography of his chest showed extensive bilateral infiltrations Necropsy revealed interstitial and intra alveolar fibrosis 2 patients died suddenly at home necropsy of 1 of them showed congestive cardiac failure 1 patient died of uræmia and 1 severely ill with uræmia died while his blood pressure was low owing to H M B treatment the hypotension was thought to have contributed to his death 1 patient died of cerebral hæmorrhage, and 2 of dissecting aneurysm of the aorta

TABLE IV—SIDE-EFFECTS IN 26 PATIENTS TREATED WITH H M B

| Symptom | None | Slight | Severe | Methonium therapy discontinued |
|---|---|---|---|---|
| Postural faintness | 16 | 0 | 3 | 1 |
| Constipation | 14 | 7 | 4 | 1 death from ileus |
| Diarrhœa | 20 | 4 | 2 | Nil |
| Visual disturbances | 20 | 4 | 2 | Nil |
| Retention of urine | 23 | 2 | 1 | Nil |
| Skin reactions | 23 | 2 | 1 | 1 |

*Control of Side-effects and Complications*

Dryness of the mouth was partly overcome by the use of acid drops Photophobia due to mydriasis was remedied with sun glasses and paresis of accommodation by special reading glasses

Constipation was usually best controlled by liquid paraffin emulsions but enemas were occasionally necessary in the early weeks of treatment Difficulty in micturition was minimised by telling the patient to empty his bladder *before* each injection More conveniently neostigmine was used to counteract the above mentioned side-effects It was usually given as neostigmine bromide 3 75–15 00 mg by mouth, but in a few cases neostigmine methyl sulphate 0 25 mg was mixed with the dose of H M B for injection

Special care was needed in dealing with patients with poor renal function H M B is lost from the body mainly by urinary excretion hence any factor which decreases the production of urine will increase the level of H.M.B in the blood and produce further hypotension with the possibility of severe oliguria or even anuria In practice this state of relative overdosage will be produced by severe diarrhœa vomiting or excessive loss of fluid through the skin owing to fever or to a hot climate. Although our patients were always warned to reduce or omit their injections and to contact one of us if diarrhœa became troublesome we lost 1 patient from ileus and peritonitis (Goldsmith 1955)

## Comparison of Soluble and Long acting Preparations of H M B

No formal comparison of the two preparations was undertaken but some conclusions are possible from our blood pressure charts and from observations on patients who had received both types of injection An increased duration of action over that of the soluble form was not a striking feature of the retard preparation The important advantage of the retard preparation lay in the diminution of unpleasant side-effects in the first hour after injection Four patients who had been controlled on soluble H M.B were changed to the long acting form, with the necessary adjustments of dosage 3 of these patients had to sit or lie down for an hour or two after injections of the soluble form owing to dizziness or exhaustion all 3 patients

TABLE V—DEATHS DURING TREATMENT WITH RETARD PREPARATION OF HEXAMETHONIUM BROMIDE

| Relationship to treatment | Case no | Cause of death |
|---|---|---|
| Due to treatment | 20 | Paralytic ileus and peritonitis |
| Possibly related to treatment | 7 | Dissecting aneurysm of aorta |
|  | 12 | Dissecting aneurysm of aorta |
|  | 10 | Cerebral hæmorrhage |
|  | 15 | "Methonium lung" |
|  | 25 | Uræmia death while B.P was low owing to H.M.B. |
| Unknown or unrelated to treatment | 26 | Uræmia |
|  | 19 | Sudden death |
|  | 21 | Sudden death |

could continue their activities without discomfort after injections of the retard form The 4th patient (case 3), whose cardiac dyspnœa was dramatically relieved by the injections, remarked that the retard form lasted longer but the soluble form acted more quickly

### Discussion

Several new hypotensive agents are now in use, but these drugs may prove fully effective only in combination with a ganglion-blocking agent It is therefore important to be familiar with the technique of treatment with drugs such as H M B It is not uncommon to meet patients who have been treated inadequately with hypotensive drugs and whose condition has continued to deteriorate owing to poor control of blood-pressure Inadequate treatment may well become more common now that several oral hypotensive drugs are available It is therefore worth emphasising that long-term outpatient treatment of severe hypertension is practicable, though troublesome and time-consuming The effectiveness of this treatment is shown by the patients' records of work Of the patients treated for more than three months 8 of 10 with benign hypertension and 4 of 7 with malignant hypertension returned to full-time work The objective results of successful treatment are most clearly seen in the complete relief of left ventricular failure in the benign group, and in the reversal of papillœdema in all the cases of malignant hypertension

Successful results with H M B therapy have been achieved mainly in patients with malignant hypertension or with benign hypertension accompanied by severe organic symptoms We failed to maintain treatment in patients with anxiety symptoms and in 1 patient who was symptom-free For such cases treatment with H M B is too rigorous and other drugs may prove more useful These patients needed treatment because they had severe hypertension with evidence of vascular damage, falling into the group described by Leishman (1953) as "accelerated hypertensive disease"

The minor side effects tend to diminish in severity as treatment becomes established, but the deaths of a patient with ileus and of a very ill patient during a period of hypotension point to the dangers of hypotensive drugs The pathogenesis of "methonium lung" (Doniach et al 1954) is not fully understood, but this condition may be a consequence of the increased life span of a treated patient with severe hypertension rather than a direct effect of methonium This complication has been recorded by Morrison (1953) and by Morrow et al (1953) in 8 patients with either malignant or premalignant hypertension Methonium lung does not appear to have been recorded previously in benign hypertension

The 2 deaths from dissecting aneurysm may possibly have been related to treatment, since the increased fluctuations of blood-pressure brought about by methonium might predispose to this and other vascular accidents

We were impressed not so much by the greater duration of action of the retard preparation as by the relative freedom from side effects in the first hour or two after injection This difference probably explains an inconsistency between our results and those of Harington and Rosenheim (1954), who, using soluble H M B, found that the fall of blood-pressure was rarely satisfactory unless the postural effect was severe enough to make the patient lie down for an hour after the injection We achieved satisfactory control without this period of incapacity, and the retard medium was probably responsible for this milder effect, which enabled patients to lead an uninterrupted working life once treatment had been established

### Summary

26 patients with severe hypertension were treated with a long-acting preparation of H M B

11 of the patients had malignant hypertension

This form of treatment is practicable for the long management of some patients with severe hyper accompanied by organic symptoms

Use of the retard medium is beneficial, since the of incapacity which follows an effective dose of the form is largely avoided

Our thanks are due to the medical, nursing, and lab staff of the Central Middlesex Hospital for their particular to Dr R A J Asher under whose care patients were treated, and to Dr K P Ball for much advice Messrs May & Baker Ltd supplied the 'Ve Retard'

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# CARBIMAZOLE IN THYROTOXICOSIS*

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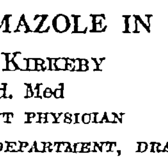
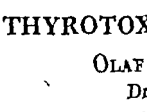
ANTI-THYROID drugs have been used for more than ten years in thyrotoxicosis Those most in use in the last few years—e g, methylthiouracil, propylthiouracil and methimazole ('Tapazole,' 'Mercazole')—have caused side effects in a relatively large number of patients symptoms of general toxicity or of oversensitivity, rash, drug fever, leucopenia, or arthralgia, and reactions of growth and increased vascularisation of the thyroid gland

New anti thyroid drugs are still being introduced among them a new compound, carbimazole ('Neo-Mercazole'), prepared by an English research team (Lawson et al 1951) This compound is derived from methimazole and differs from it only by a carbethoxy group which blocks the active thiol group



CARBIMAZOLE



METHIMAZOLE

The anti-thyroid effect of carbimazole is presumably the result of hydrolysis with gradual release of a compound identical with methimazole It was hoped that carbimazole would give a more constant supply of the active material to the thyroid gland than that which could be obtained by administering methimazole This would make it possible to reduce the dosage and thereby to lessen the risk of side effects The introduction of the carbethoxy group rendered carbimazole tasteless in contrast to the other anti thyroid drugs

The anti-thyroid potency of carbimazole, investigated experimentally by Macgregor and Miller (1953) with radioactive iodine by the technique of Stanley and Astwood (1947), proved slightly more potent than that of methimazole In clinical experiments also carbimazole proved to be a very active anti-thyroid remedy (Doniach

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* Read at the Norwegian Society for Internal Medicine, Oslo on Oct 4, 1954

53 Poate 1953, Bartels 1953) Some rkers did not notice any side-effects, t of the 52 patients of Bartels (1953) 1 veloped agranulocytosis and 2 had skin ections, and Harrison (1954) reported ase of agranulocytosis

It has been claimed that carbimazole es not cause hyperplasia of the thyroid nd to the same extent as other anti yroid drugs Poate (1953) using carb azole preoperatively, confirmed this in few cases, but Doniach (1953) found itrogenic reactions in 7 of 120 patients Up to now very little has been pub hed about carbimazole therapy the mber of cases not exceeding 400 erefore our experience of carbimazole erapy in the medical department of ammen Hospital may be of interest

## Clinical Materials and Methods

Carbimazole has been used at Drammen spital since July, 1953 During this riod 56 patients with thyrotoxicosis— women and 6 men—have been treated th it. The patients were aged 22–79 erage 48 The diagnosis was made in e usual way Several estimations of sal metabolic rate (B.M.R.) were made fore the start of treatment the serum olesterol level was determined in all the patients and some cases where the diagnosis was doubtful it was nfirmed by using radioactive iodine The treatment as started in hospital and usually continued in e outpatient department every three or four weeks e patients were followed up for up to sixteen onths

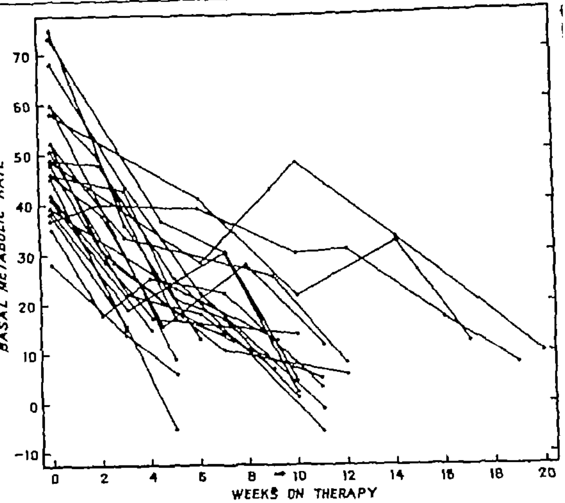
In 29 patients thyrotoxicosis had been recently diag sed; 10 had relapses after previous operations 13 d relapses after earlier treatment with either methyl iouracil or propylthiouracil 3 had been treated with ethylthiouracil and the B.M.R. had become normal t goitrogenic reactions had developed; and in 1 case opylthiouracil therapy had caused drug fever In 46 tients a goitre was palpable

To obtain data for comparison regarding the develop nt of a goitre during treatment we examined the spital records of 38 patients treated with either methyl iouracil or propylthiouracil at the same hospital in the riod Jan 1 1952 to June 30 1953

## Results

The lowering of the B.M.R by carbimazole was very tisfactory In most cases the B.M.R. fell to normal in -12 weeks average 6 weeks. 4 cases responded slowly t were finally controlled after 3–5 months The cause of this slow response was probably insufficient initial dosage In 1 case we could not restore the B.M.R to rmal, but this patient had in addition to her thyrotoxicosis (confirmed by using radioactive iodine) congenital heart-disease The return of the B.M.R towards normal in the first 23 patients is shown in the accompanying figure

A very rapid subjective improvement took place in nearly all the patients Weakness nervousness and palpitations disappeared in a short time the patients gained weight and the pulse rate became normal The serum-cholesterol level rose as the B.M.R. fell Doniach (1953) maintained that a rise of serum-cholesterol level of more than 40% above the initial value was a sign of overdosage but we have been unable to confirm this In 9 cases we observed an increase of over 40% but only in 2 of these patients were there slight signs of overdosage



Return of B.M.R. towards normal in 23 patients treated with carbimazole.

In the published reports there is no agreement about the initial dosage Lawson and Barry (1951) maintained that 10 mg daily was sufficient, but this has not proved valid. Since then much higher doses have been recommended Doniach (1953) considered 15–20 mg to be an adequate initial dose for mild cases with small goitres but recommended 30 mg for cases of average severity and 40–45 mg for severe cases with large goitres Bartels (1953) found the small doses insufficient to bring about a satisfactory clinical response and claimed that 30–50 mg daily was required, according to the type and size of the goitre to be treated

Our experience confirms what Bartels said In some of our first cases we gave 15 mg as the initial daily dose but in most of them we had to increase the dose to get a satisfactory response Later we used 30 mg in mild cases and 40 mg in severe ones, and in 2 cases we increased the dose to 60 mg A comparison of the fall in B.M.R. in the two groups of patients receiving 30 mg and 40 mg shows the higher dose to have given the more favourable response The average fall of B.M.R in the two groups was 0-6% and 0 9% a day respectively indicating that 40 mg is the optimal dose in most cases

We found that the usual maintenance dose necessary to keep the B.M.R. between 0 and +15% was 5–10 mg a day

*General side-effects* were seen only in 1 case where carbimazole had to be discontinued because of a rash

*Goitrogenic reactions* were seen in 4 patients a considerable goitre developed in 1 case and in a further 3 cases there was a slight increase in the size of the thyroid gland, rapidly reverting during continued treatment Usually a goitre decreased in size under treatment this was so in 3 cases in which carbimazole was substituted for methylthiouracil because of increasing goitre In comparison with this goitrogenic reactions developed in 13 of 38 patients during treatment with either methyl thiouracil or propylthiouracil (in 4 of them the drug had to be discontinued for this reason) The B.M.R in the patients was above 0 during the period in which increase of goitre was observed The incidence rate of this complication was therefore 34% in the cases treated with either methyl thiouracil or propylthiouracil compared with 7% in those treated with carbimazole

## Discussion

The fact that the initial dose used in the treatment with carbimazole—i e , 30–50 mg daily—is also the dose used for patients given methimazole may seem disappointing The theoretical assumption regarding carbimazole was that smaller doses might suffice to control the overactivity of the thyroid gland The structural formula (see above), however, shows that this is so A great part of the molecule of carbimazole is occupied by the carbethoxy group, and the molecular weight of this material is therefore considerably greater than that of methimazole—186 and 114 respectively The hydrolysis of 40 mg of carbimazole liberates only 25 mg of the active compound, methimazole, and the real dose is thus reduced correspondingly

The importance of this is evident from previous experience with anti thyroid drugs The incidence rate of side effects has, to a considerable extent, depended on the dosage, particularly as regards the serious complications affecting the bone-marrow In methimazole treatment the most severe toxic reactions developed in patients taking large doses, and 9 patients who developed agranulocytosis during this treatment received on an average 47 mg daily (McGavack and Chevalley 1954)

Carbimazole, with its lower content of active substance, should therefore produce fewer side effects This seems to be true, but many more patients must be treated with *carbimazole before we can give a decisive answer to this* question Fraser et al (1954), comparing the incidence rate of toxic reactions due to larger doses (60 mg daily) of methimazole and carbimazole, found side effects in 6 of 22 patients and only 1 of 41 patients respectively

The claim that carbimazole tends less than other antithyroid drugs to produce goitrogenic reactions remains unexplained, but Rawson (1954) believes that the thyroid-stimulating hormone (T S H ) of the pituitary gland is normally inactivated by oxidation in the thyroid gland He states that thyroid tissue in vitro will inactivate added T S H , but the activity is restored by adding a reducing agent, such as thiouracil It may well be that carbimazole, in which the reducing –SH group is protected by substitution, either does not reactivate T S H or does so only slightly, according to the degree of hydrolysis and liberation of free –SH

## Summary

56 patients with thyrotoxicosis were treated with carbimazole

52 received it as curative treatment and 4 as preoperative preparation

Most of the patients became euthyroid within 3–12 weeks

Side effects were observed in only 1 case, in which the carbimazole had to be discontinued because of a rash

Goitrogenic reactions developed in 7% of the patients, compared with 34% of 38 patients treated with either methylthiouracil or propylthiouracil

Carbimazole seems to be just as effective as the more commonly used anti-thyroid drugs and substantially less toxic than these

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# THE ESTIMATION OF NEUROSIS*

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NEUROSES range in gravity from the complete incapacitating to the mildly annoying, shading imperceptibly into normality As Hoch and (1954) have pointed out, there is great need for standardised method of assessment which could applied to neurotic patients and used in the evaluation of various forms of therapy In such follow up as have been carried out it has been usual to class the patients in such categories as "recovered, "improved," and "slightly improved," without any real attempt to equate their condition at the be and end of treatment In many papers these categ are defined in static terms, although they should be related to the starting point A peculiarity of some psychotherapists' definitions is that they make prophecies as to how the patient will react to stress future and make use of vague conceptions, such as inherent strength of the patient's personality S times these predictions are rather like the figures over confident parson might produce if he were how many of his flock were destined for hell fire how many souls he had saved by his own personal

A good example of what happens when compari are made between series of statistics prepared in th way is afforded by Denker (1946) He examined reports from various psychiatric clinics in many countries and concluded that in most of them the proportion of pati who recovered or were very much improved was betwe 40% and 70% He compared this with the results of general practitioners' treatment of 500 patients who had claimed disability benefit from an insurance compa because of neurotic illness, and found that the percentage was very much the same *From this* he concluded th the general practitioners did on the whole as well f their patients as the psychiatrists, and that specialised psychiatric treatment for neurotics was not of obv value To anyone experienced in follow up studies of neurotic patients the fallacy behind this is appare In the insurance-company cases the criterion of cure improvement was return to work and ability to earn th own living , but many of the clinic patients had sou help for neurotic symptoms and personality difficul which had never prevented them from working It is general much easier to secure *some sort* of work adju ment for a neurotic than to relieve him of his symptom or to alter his personality in any fundamental way other words the types of patient and the therapeu goals were so utterly different in the various se produced by Denker that no conclusions are possible

I shall now describe a system which I first used sixte years ago (Harris 1938) and which I have found serv able both for the study of the natural history of neuro illnesses and for comparison of the results of differe methods of treatment (Harris 1954) It depends essentially on social adaptation, which seems to be th fundamental problem of neurosis and is the criter usually applied by the layman There are four grade

1 Unable to pursue their occupations on account of symptoms and consequently an economic burden on the families or the community

2 Able to work and earn a living but forced by the symptoms to modify their lives considerably, resulting in much limitation of their interest and activities

3 Able to lead full active lives, but at times serious inconvenienced by symptoms

4 Free from symptoms and apparently well

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* Presented to the Fifth International Congress on Mental Health, Toronto, August, 1954

he distinction between grades 1 and 2 is usually very y the only difficulty arises in the case of house es, and where someone else has to carry out the ater part of their housewifely duties for them I e put them in grade 1 The essential characteristic grade 2 is restriction of activity by symptoms—bility to travel or to go out alone fear of mixing h people, leading to the dropping of healthy social ntacts fatigue necessitating excessive periods of t intolerance of crowds closed spaces, cinemas and e like. Sometimes one has to evaluate such a symptom occasional headache the consideration there being ether *the* patient regards himself as ill and in need of atment (in which case he is put in grade 3) or not which case he is put in grade 4) Although the measure a rather coarse one, and substantial degrees of improve ent can occur without being reflected in the grading the ethod has the advantage that it is easy to apply, quires a minimum of psychiatric knowledge, gives ally very little scope for disagreement in the grading individual patients and could readily be used by a rse or social worker While there is obvious scope for provement it would be a mistake to make it more aborate either by increasing the number of grades in other ways for excessive complexity is a pitfall the construction of classifications of this type.

In making this objective assessment it is desirable the same time to record the opinion of the patient—hether he feels that the treatment has been helpful not. The two assessments are sometimes strikingly variance and patients occasionally attribute their nprovement apparently with justification to extraneous ctors The patients come for help and it is important know whether they think that they have received it

When a therapeutic method is to be tested both the reliminary grading and the later ones should be done y someone other than the doctor carrying out the reatment since he is in danger of becoming overloaded ith detail and of developing an emotional bias

My approach implies a limited therapeutic aim which ome psychotherapists will regard *as too low* but it eems to me that we must be realistic and beware of ttempting the impossible

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# A SIMPLE METHOD OF TESTING TASTE

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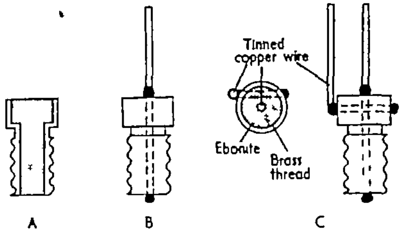
THOUGH the indications for testing taste are rare, the occasions on which such a test is done are very much rarer Probably this is because the traditional way of testing taste—namely by dropping weak solutions of sugar, common salt quinine and acetic or other acid on to the lateral border of the tongue—is both fiddling and laborious

It has long been known that a weak electric current when applied to the tongue causes a sensation which is in fact that of taste I have put this knowledge to practical use in the following simple apparatus in which the electric current comes from an ophthalmoscope battery

## Apparatus and Method

The instrument was constructed for use with a Lister Morton ophthalmoscope (A pocket torch or similar appliance would serve the purpose equally well ) The bulb only was adapted and may be replaced by an ordinary illuminating bulb as occasion arises



The globe and filament of the electric bulb were removed, and the central porcelain was replaced by a plug of ebonite which fitted into the tin plated brass forming the shell of the bulb (fig A) A central hole size 55 was drilled in the ebonite and into this a piece of 16 s w g tinned copper wire was fixed by means of a blob of solder at either end (fig B) The ebonite centre was secured in the brass thread by a similar wire soldered to it at right angles to the first. This was then bent parallel to the first wire so as to form the second electrode (fig C)

With the current switched off, the electrodes are applied lengthwise to one or other side of the anterior two thirds of the protruded tongue, so that about 1 cm of each electrode is in contact Slight pressure should be applied to make the contact firm The patient is asked to appreciate the sensation thus experienced (namely, that of the two electrodes touching his tongue) and subsequently he is asked to indicate for example with a grunt whether he is aware of any additional sensation Some seconds later the switch of the ophthalmoscope is turned on and instantly another sensation is normally experienced

The descriptions given by patients of this sensation vary, but it is believed to be purely that of taste When it is absent, taste is absent. Though it is easiest to test the antero lateral border of the tongue, taste should not be pronounced absent until the tip also has been tested

## Observations

The more precise descriptions given by patients of the sensation include those of something acid or something metallic, and one patient spontaneously affirmed that it was an electrolytic taste Patients often say that they feel something like an electric current and this, among other things presumably accounts for the belief that what is being tested is or at any rate includes, common sensation There is evidence that this is not so When for example the current is applied elsewhere than on the tongue—e.g inside the mouth or on the lips—no additional sensation is experienced On the appropriate area of the tongue the additional sensation is normally experienced when the ophthalmoscope switch is at the position where the filament of the bulb would only just glow the current which is passing across the tongue in these circumstances amounts to 120 microamps

Further evidence of the specificity of this test for taste comes from the following observations

(1) A patient with a peripheral facial palsy who stated that taste had been lost on one side had no impairment of ordinary sensation in the trigeminal distribution on the same side He had no additional sensation whatever when the appropriate stimulus was applied yet it was this same patient who when the unaffected side of his tongue was tested explicitly described an electrolytic *taste*

(2) A patient had an alcohol injection of the gasserian ganglion for trigeminal neuralgia, with resultant complete analgesia and anæsthesia of trigeminal distribution He was unaware of the preliminary application of the electrodes to his tongue but when the current was switched on he instantly experienced a sensation

These observations have been repeated on several occasions In cases with complete analgesia and anæsthesia the sensation has been described as "numbness" or "a pricking sensation"

Where both the conventional method and this one have been used, the results have in general coincided Occasionally, however, testing with salt and sugar only has indicated an absence of taste, while subsequent testing with the electrodes has shown that the sensation was present and apparently normal Further tests in these cases have shown that the taste of acid and quinine could be appreciated In no case has taste been found absent by this method but present by other methods

### Discussion

These observations suggest that taste alone is being tested The patient's description of the sensation experienced is, of course, irrelevant, since the significance lies solely in whether the sensation is present or not, and this may be determined within less than half a minute of deciding to do the test

To demonstrate the *degree* of impairment may, however, not be so easy, yet in patients in whom taste was returning, the intensity of the *additional sensation* has been found to be less than on the unaffected side The method cannot, of course, differentiate between the various primary tastes This might imply that the method is crude, it also suggests that the conventional method is equally unreliable for distinguishing degrees of impairment Both methods rely, of course, on the intelligent cooperation of the patient, but the method described seems to be less exacting

### Summary

A simple and rapid method of testing taste is described Presence or absence of taste can readily be demonstrated Less satisfactory are the conclusions that can be drawn regarding degrees of impairment

My thanks are due to Mr E Dennis of the physics department, Guy s Hospital, for making the device, and to the department of medical illustration for drawing it

# RENAL TUBULAR FAILURE ASSOCIATED WITH POLYARTERITIS NODOSA

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M D Lond, F R C S, D T M & H

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Polyarteritis nodosa is associated with a wide variety of renal functional disturbances These can usually be related to necrotising glomerulitis or to multiple renal infarctions secondary to the characteristic arterial lesions The case described here was unusual in that functional changes were due to tubular insufficiency and that the structural changes in the non infarcted areas were confined mainly to the tubules

### Methods

Blood samples were collected from the antecubital vein and placed into tubes containing heparin Urine collections were made on urine passed naturally, except when the effect of 'Pitressin' was studied, a catheter was then introduced into the bladder some hours before the test was done

TABLE I—PLASMA CONTENT OF SODIUM, POTASSIUM, CH
CARBON DIOXIDE, CALCIUM, PHOSPHORUS, MA
UREA, AND CREATININE

| Day no | Sodium * | Potassium * | Chloride * | $CO_2$ * | Calcium * | Phosphorus * | Magnesium * | Urea † | [illegible] |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 127 | 3 4 | 79 | 32 | | | | | |
| 2 | 132 | 3 4 | 82 | 32 | 5 0 | 2 0 | | [illegible] | |
| 3 | | | | | | | | | |
| 4 | 120 | 2 7 | 75 | 32 | | | | | [illegible] |
| 5 | 135 | 3 9 | 89 | 27 | | | | [illegible] | |
| 6 | 133 | 4 2 | 94 | 24 | | | | | |
| 7 | 122 | 5 9 | 88 | 25 | | | | | [illegible] |
| 8 | 127 | 4 2 | 89 | 27 | | | | | |
| 9 | 131 | 5 0 | 82 | 33 | 3 9 | 1 3 | 1 3 | | |
| 10 | 136 | 4 7 | 91 | 33 | | | | | [illegible] |
| 11 | 129 | 4 6 | 87 | 29 | 6 8 | 3 1 | | | [illegible] |

* m eq per litre † mg per 100 ml

The analytical methods were as follows sodium potassium, flame photometer, calcium, permanga titration (Clark and Collip 1925), magnesium, phos precipitation (Briggs 1924), phosphate, (Fiske and Subbarow 1925), chloride, thio titration (Van Slyke 1923), bicarbonate, volum (Peters and Van Slyke 1922), urea, urease met (Van Slyke and Cullen 1916), creatinine, co (Bonsnes and Taussky 1945), osmolarity of urine cryoscopy (depression of freezing-point in Centigrade — by 1 86=osmols per litre) with a therm meter graduated in 0 01°C

### Case-report

The patient, a woman aged 31, was admitted to h complaining of thirst, polyuria, and headaches A year b admission she had had a five-day fever which was th to be influenza but which, for two weeks, was associated œdema of the ankles For nine months before admission had had to get up at night to pass water, and for the eight weeks she had had severe fronto occipital heada nausea, and vomiting For six weeks there had been polyuria and polydypsia both day and night These symp had persisted and she had become weak and tired and about one stone in weight In the two weeks before adm she had had occasional severe pain in the loins, and the past week two attacks of unconsciousness followed time by restlessness and confusion for twenty four hours denied feeling feverish, though she stated that she had occasional shivers for about a week At the age of 1 had had an illness suggestive of acute nephritis from wh she had made a complete clinical recovery When she was years old she had toxæmia of pregnancy, with œdema hypertension, she recovered after the spontaneous deliv of a stillborn infant at 7 months

*On examination* the patient looked ill, physically leth and shrunken with hollow eyes and loss of skin elastic Mentally she was alert and apprehensive The jugular ve pressure was *normal and there was no* œdema, heart ra 100–110 per min, regular, blood pressure 160/130 mm. H the apex beat was in the sixth intercostal space, just beyo the midclavicular line The tongue was dry and dirty, the was moderate tenderness in the loins and generalised abdom discomfort on palpation of the anterior abdominal wall, th spleen was not palpable There were no abnormal phys signs in the central nervous or respiratory systems Th retinal vessels appeared normal Oral temperature was norm

*Investigations*—Urine *specific gravity* 1002, protein 3 5 g per litre (Esbach), on microscopy there were a moder number of nucleated cells and occasional red cells Hæmo globin 14 8 g per 100 ml, white blood cells 11,000 per c.mm (polymorphs 9790 per c.mm [89%], lymphocytes 110 per c.mm [10%], monocytes 110 per c.mm [1%]), packed-cell volume 45% Erythrocyte sedimentation rate 107 mm. in the 1st hour (Westergren) Plasma proteins 6 1 (albumin 2 globulin and fibrinogen 3 5) g per 100 ml, the electrophoret pattern was albumin 32%, globulins $\alpha_1$ 4 5%, $\alpha_2$ 27 7%, β 8 1 and γ 22 5% Plasma electrolytes are shown in table I, the main feature on admission was a metabolic alkalosis with a net decrease in sodium and chloride and a less pronounced in potassium plasma-calcium was 5·0 m eq per litre trocardiography showed appearances characteristic of adium deficiency with ST depression and a widened T wave ging with a prominent U wave there was also left icular preponderance Radiographs of chest skull long s, and abdomen showed no abnormality

*rogress*—During the first few days headaches nausea vomiting were severe and continuous Nausea and vomit- responded to chlorpromazine, but there was no return of tite The heart rate gradually rose and there was an ting temperature of 99°–100°F It became obvious that e was a severe urinary loss of water and electrolytes and the fourth day onwards it was decided not only to endea- r to keep pace with the current loss, but also to try and ieve a positive balance The oral and intravenous adminis- ion of very large quantities of electrolytes in the next 6 days was accompanied by a corresponding increase in nary loss which so nearly equalled the intake that only nor positive balances resulted.

LE III—URINARY OSMOLARITY AND SOLUTE EXCRETION RATE

| no. | Collection period (min.) | Urine flow (ml. per min ) | Osmolarity of urine (milli-osmols per litre) | Solute output (micro-osmols per min ) |
|---|---|---|---|---|
| 3 | 1440 | 4·45 | 227 | 1010 |
| 4 | 1440 | 8·3 | 167 | 1390 |
| 5 | 90 | 13·4 | 230 | 3080 |
| 6 | 1440 | 5·25 | 216 | 1130 |
| 7 | 20 | 2·8 | 175 | 490 |
|  | 10 | 2·0 | 212 | 550 |
| 8 | 120 | 8·7 | 199 | 1733 |
|  | 1440 | 8·4 | 216 | 1800 |
|  | 21 | 13·9 | 207 | 2800 |
| 9 | 1440 | 8·0 | 200 | 1600 |
| 10 | 1440 | 5·2 | 266 | 1380 |
| 11 | 1200 | 2·3 | 263 | 605 |

On the sixth day a more determined effort to replace tassium resulted in a substantial positive balance of both tassium and water On the 7th day the tongue was moist d the patient stated that for the first time in many weeks e was less thirsty A few hours later however she developed form of tetany which was relieved only temporarily by travenous injections of calcium chloride These attacks of tany were frequently associated with hyperventilation, vere retrosternal pain and such an accentuation of appre nsion that she was liable to panic Retrosternal pain was severe that it made her cry out, and it had to be controlled morphine Occasionally this triad of pain hyperventila on and panic occurred without overt evidence of tetany here was no oedema rise in jugular venous pressure or ugh.

By the eighth day the packed-cell volume had fallen and ill a pint of packed red blood-cells was given This only ovoked cardiac failure with a heart rate of 180 per min. allop-rhythm a rise in jugular venous pressure to 5 cm. bove the sternal angle tender enlargement of the liver and vere dyspnoea Recovery occurred within a few hours of eatment with digitalis and aminophylline Between the ghth day after admission and death three days later the patient was given 200 mg of cortisone by mouth each day This treatment was associated at first with a large negative balance of sodium and chloride and a positive balance of potassium and clinically she seemed to improve slightly On the following day however there was a large negative potassium balance and a small loss of sodium. Intermittent attacks of tetany continued and on the ninth day plasma calcium was 3 0 m.eq per litre; during the next twenty four hours there were repeated attacks of tetany and 4 g of calcium gluconate was given intravenously; there were no further attacks during the last two days of life During the last thirty-six hours severe chest pain recurred from time to time associated with hyperventilation and attacks of panic Twelve days after admission the patient died suddenly during one of these episodes, complaining terminally of intense paræsthesiæ in the hands There was no evidence of tetany; Chvostek's and Trousseau's signs were negative and the plasma calcium was 6·8 m eq per litre Plasma protein concentrations were essentially the same as on admission.

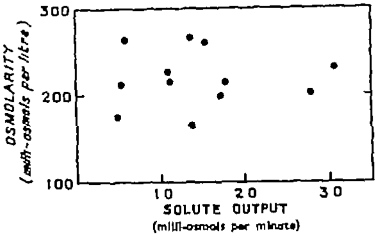


Fig 1—Relation of urine osmolarity to solute-excretion rate

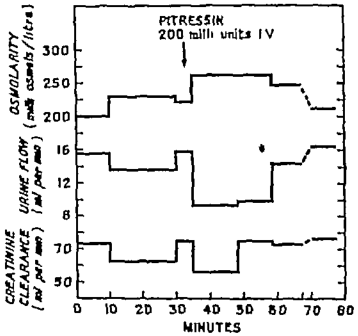


Fig. 2—Effect of intravenous pitressin 200 milli-units on creatinine clearance and urine osmolarity and flow during an infusion of 1 8% saline.

TABLE II—DAILY 24 HOUR BALANCE AND URINARY OUTPUT (SEE TEXT) OF WATER, SODIUM, POTASSIUM AND CHLORIDE, AND 24 HOUR CREATININE CLEARANCE AND SODIUM PLASMA URINE (P/U) RATIO

| Day no. | Fluid |  |  | Sodium |  |  |  | Potassium |  |  | Chloride |  |  | Creatinine |  |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|  | Oral and I.V. intake (litres per 24 hr ) | Urine output (litres per 24 hr ) | Balance (litres per 24 hr ) | Urine |  | Balance (m.eq per 24 hr ) | P/U ratio | Urine |  | Balance (m eq per 24 hr ) | Urine |  | Balance (m eq per 24 hr ) | Urine output (mg per 24 hr ) | Clearance (ml per min ) |
|  |  |  |  | Conc (m.eq per litre) | Output (m eq per 24 hr ) |  |  | Conc. (m.eq per litre) | Output (m.eq per 24 hr ) |  | Conc. (m.eq per litre) | Output (m.eq per 24 hr ) |  |  |  |
| 2 | 6·1 | 6·4 | −0·3 | 62 | 307 |  | 2·1 | 46·0 | 291 |  | 57·4 | 367 |  | 770 | 53 |
| 3 | 7·6 | 3·8 | +3·8 | 60 | 226 |  |  | 45·0 | 171 |  | 63·0 | 230 |  |  |  |
| 4 | 13·2 | 12·0 | +1·2 | 57 | 681 | +183 | 3·3 | 16·5 | 198 | +59 | 59·0 | 708 | +477 | 875 | 65 |
| 5 | 13·6 | 15·6 | +3·0 | 78 | 1217 | −66 | 1·7 | 23·5 | 367 | −15 | 89·0 | 1388 | +43 |  |  |
| 6 | 12·8 | 7·0 | +6·0 | 47 | 433 | −225 | 4·3 | 36·0 | 274 | +371 | 74·0 | 569 | +183 | 980 | 52 |
| 7 | 7·3 | 3·7 | +1·0 | 34 | 184 | +216 | 3·6 | 48·0 | 274 | −73 | 56·0 | 316 | +98 | 880 | 56 |
| 8 | 8·6 | 11·9 | −2·0 | 122 | 1315 | −1183 | 1·0 | 6·7 | 74 | +80 | 63·0 | 693 | −459 | 880 | 50 |
| 9 | [illegible] | 8·7 | −0·2 | 68 | 593 | −219 | 1·9 | 6·0 | 539 | −310 | 50·0 | 613 | −59 | 700 | 40 |
| 10 | [illegible] | 6 | −2·0 | 76 | 577 | −187 | 1·8 | 51·0 | 355 | −143 | 41·0 | 312 | +159 | 700 | 53 |
| 11 | 1·2 | 3·3 | +1·6 | 55 | 181 | +50 | 2·3 | 45·0 | 148 | −13 | 59·0 | 193 | +81 | 700 | 49 |

### ELECTROLYTE DISTURBANCES

Plasma and urine concentrations of electrolytes, urea, and creatinine, their urinary rate of excretion, and the daily balance of water, sodium, potassium, and chloride are shown in tables I and II

Balances are calculated from intakes which include only those substances given intravenously or by mouth, when particularly prescribed and known to have been ingested Dietary contents of electrolytes are not included, this was not an important factor, but the intakes are therefore underestimated The output refers only to urinary losses, no allowance has been made for insensible loss of fluids or for electrolyte losses in the fæces or sweat, the patient, however, was constipated and did not sweat perceptibly

*Sodium, Chloride, and Water*

There was a large urinary loss of sodium, chloride, and water associated with a decreased concentration of sodium and chloride in the plasma On the second and third days after admission, when no attempt was being made to replace electrolytes, and the only intake of food and drink was water flavoured with fruit juices, there was a urinary excretion of 625 m eq of sodium, 606 m eq of chloride, and 10 2 litres of water In the next two days 2034 m eq of sodium and 2616 m eq of chloride were given, but there was a positive sodium balance of only 133 m.eq, while 510 m eq of chloride was retained

Subsequently the rate of sodium chloride administration was decreased, and instead an attempt was made to produce a large positive potassium balance in the hope that this might in turn promote a greater retention of sodium and chloride A transient positive balance of potassium was achieved on the sixth day, but this did not seem to influence the retention of sodium and chloride

Eight days after admission there was an exceptionally large negative balance of sodium and chloride, on this day digitalis and aminophylline were given, and it was the first day of cortisone administration

The packed cell volume on the fourth day after admission was 45%, and the volume fell to 22% on the sixth day during the retention of about 8 litres of water (excluding insensible loss), subsequently there was a negative water balance and the packed-cell volume returned towards the initial value

*Potassium and Carbon Dioxide*

There was a substantial urinary loss of potassium associated initially with a low plasma potassium level (3 4 m eq per litre) and a high plasma $CO_2$ (32 m eq per litre) On the sixth day a positive potassium balance of 371 m eq was achieved by the administration of 645 m eq of potassium given intravenously (483 m eq ), and by mouth (162 m.eq ) By the end of this period of potassium retention plasma potassium had risen to 5 9 m eq per litre and the plasma $CO_2$ was 25 m eq per litre The plasma $CO_2$ level, however, had already fallen to 24 m eq per litre on the previous day in association with a large positive chloride balance During the last three days there was again a negative potassium balance

When cortisone was first administered there was a transient positive potassium balance for the first twenty four hours, followed by a large negative balance

*Calcium and Phosphorus*

The data on the calcium and phosphorus changes are small On the second day after admission plasma calcium was 5 0 m eq per litre and plasma phosphorus 2 0 m.eq p litre On the fourth, fifth, and sixth days calcium and pho phorus urinary excretion were as follows

| *Day* | *Calcium* (*m eq per 24 hr* ) | *Phosphorus* (*m.eq per* 24 *hr*) |
|---|---|---|
| 4 | 47 | 58 |
| 5 | 36 | 49 |
| 6 | 34 | 22 |

These figures probably represent a substantial negative calc balance since during this time hardly any food was being ea and urinary calcium excretion on a normal diet is 5–10 m per 24 hr

On the seventh day the patient developed tetany, which wa treated by repeated injections of calcium chloride intrav ously Plasma calcium and phosphorus estimations were repeated until the ninth day, when the concentrations w found to be 3 9 m eq per litre and 1 3 m.eq per litre resp tively, on this day tetany was still present On the tenth d 4 g of calcium gluconate was given intravenously, teta did not recur Ten minutes before death the plasma calc and phosphorus were 6 8 m eq per litre and 3 1 m eq p litre respectively

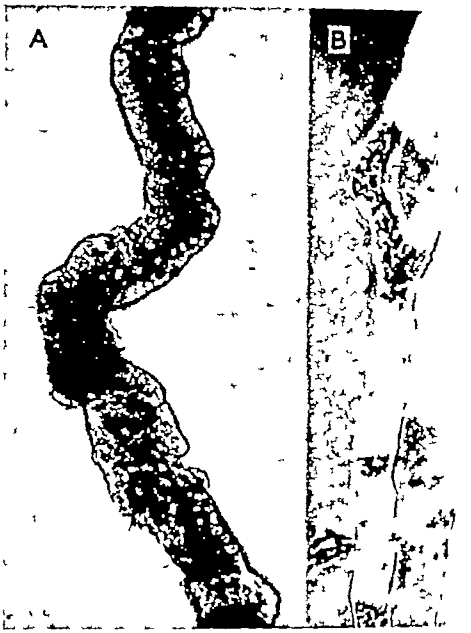


Fig 3—Phase-contrast microphotographs of tubules dissected normal kidney A, normal proximal tubule, B, normal and collecting (left) tubules. Note the regular nuclear patter clear-cut outline ( × 140 )

### RENAL FUNCTION

*Glomerular Function*

Glomerular filtration rate, measured by 24 hr endogenous creatinine clearance, varied from 45 to 55 ml per min Plasma creatinine was 0 9–1 1 mg per 100 ml and blood urea 21 and 17 mg per 100 ml

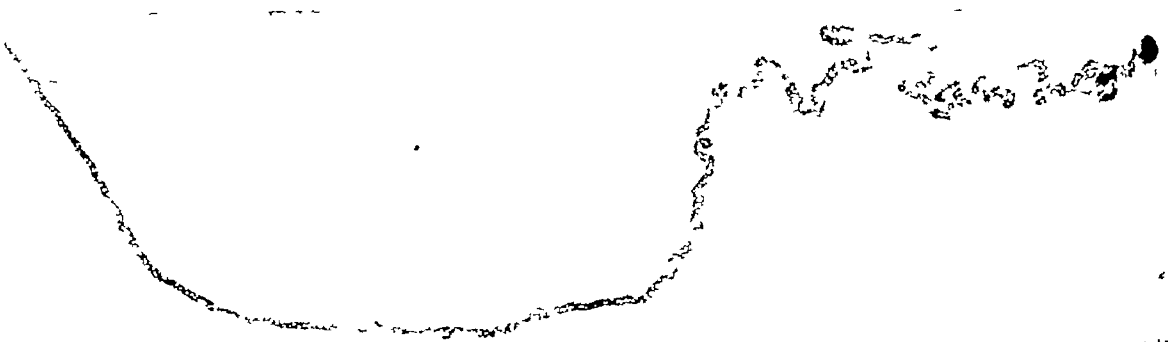
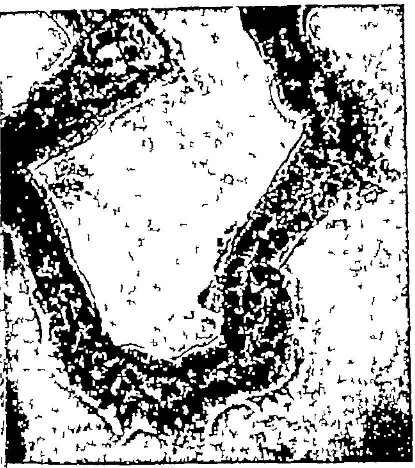


Fig 6—Mosaic of a complete proximal tubule from a non-infarcted area showing patchy areas of increased translucency flattening of the epithelium, and dilation of the lumen ( × 17)



7—Phase-contrast microphotograph of a proximal tubule at high power showing areas of increased translucency regeneration, irregular outline, and disorganisation of the nuclear pattern ( × 170)

*ubular Function*

*Electrolyte excretion.*—The large negative balances of sodium tassium chloride and probably calcium, when their con ntrations in the plasma were low indicate an extensive pairment of tubular function as regards electrolytes. This also evident from the almost fixed sodium plasma : urine tio, which fluctuated only between 1 and 3 6 while the enty four hour urine volume varied between 3 3 and 15 6 tres.

*Water excretion and concentrating ability*—The osmolarity the urine varied between 165 and 260 milli osmols per litre asma osmolarity was not estimated but the plasma-sodium ncentrations (table I) were such that it is reasonable to infer at plasma osmolarity was usually higher than that of urine able III shows the daily estimations of urine osmolarity g. 1 shows how the osmolarity of the urine remained hypo- nic and within narrow limits over a range of solute output arying from 300 to 3080 micro-osmols per min It also shows hat as the solute output increased the urine osmolarity showed o directional trend

Fig 2 illustrates the effect of the administration of 200 illi-units of pitressin intravenously on the urine osmo larity urine flow and endogenous-creatinine clearance during rapid infusion of 1 8% saline It shows that this large dose of itressin produced only a minor and very transient change in rine osmolarity from 230-260 milli-osmols per litre as the lasma sodium level was 141 m eq per litre at this time it is nlikely that the urine osmolarity reached that of plasma.

*Proteinuria*

Protein was present at all times, in amounts varying between a trace and + + + depending on the urine volume Using Esbach's method for the estimation of urine protein concentration the 24 hr excretion rate of protein was estimated once (on the third day) when it was 11 4 g

## POST MORTEM FINDINGS

A post mortem examination was performed four hours after death. The external appearances were of a normally developed young woman with extensive tanning of the exposed areas of skin due to sunlight The principal findings included hypertrophy of the left ventricle of the heart (total weight 310 g ) and a confluent approximately wedge-shaped zone of caseous tuberculosis in the lower lobe of the left lung which measured 6 cm. at its widest Beyond the main tuberculous focus were several outlying small daughter tubercles There were pulmonary emboli in the lower lobe of the right lung probably derived from bilateral thrombosed calf veins in the legs Microscopic examination showed fibrocaseous tuberculosis and an early red infarct in the lungs, and a fibrocaseous tuberculous focus in the spleen No conspicuous abnormalities were found elsewhere, except in the kidneys.

*Kidneys*

The kidneys were smaller than normal and weighed 140 g each. Beneath the capsules, which stripped with ease there were extensive scars due to infarcts in varying stages of repair The cortex between the infarcts was swollen and yellowish Examination of the main renal arteries and their immediate divisions showed no evidence of an embolus or other local arterial disease

*On section* there were extensive lesions throughout the kidneys consisting of wedge shaped infarcted zones involving both cortex and medulla. In these areas damage varied from complete destruction to tubular atrophy partial glomerular shrinkage and much interstitial chronic inflammatory-cell infiltration In the non infarcted zones there were scattered glomerular lesions and widespread dilatation and fatty degeneration of the tubules as shown in fat-stained sections Some of the glomeruli were swollen and avascular with the tufts slightly fibrosed a few contained microthrombi in the glomerular capillaries.

The larger arteries were in some instances, almost completely blocked by intimal fibrosis, while the medial coat showed segmental disruption (fig 5) intralobular arteries occasionally showed fibrinoid changes that extended into the surrounding tissues (fig 4) Both appearances were typical of those found in polyarteritis nodosa. The smaller afferent glomerular arteries displayed the features normally seen in malignant hypertension and fibrinoid change extended into the base of the glomerular tufts. No similar arterial changes were found in other organs

The appearances of the large renal vessels were compatible with healing and healed polyarteritis nodosa those in the smallest arteries were more in keeping with malignant hypertension The absence of malignant hypertensive changes in other organs, however and the very close relationship in the histological changes of both conditions, suggests that all the arterial changes can be explained on a basis of polyarteritis nodosa alone The absence of arterial changes elsewhere than

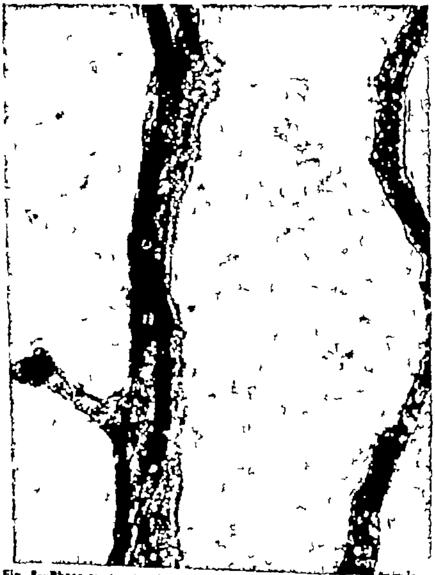


Fig. 8—Phase-contrast microphotograph of a distal tubule (extreme right) and collecting tubule (left) showing epithelial necrosis, regeneration, and dilation of the lumen with occasional cast formation. The distal tubule shows minimal changes in its epithelial pattern ( × 150.)

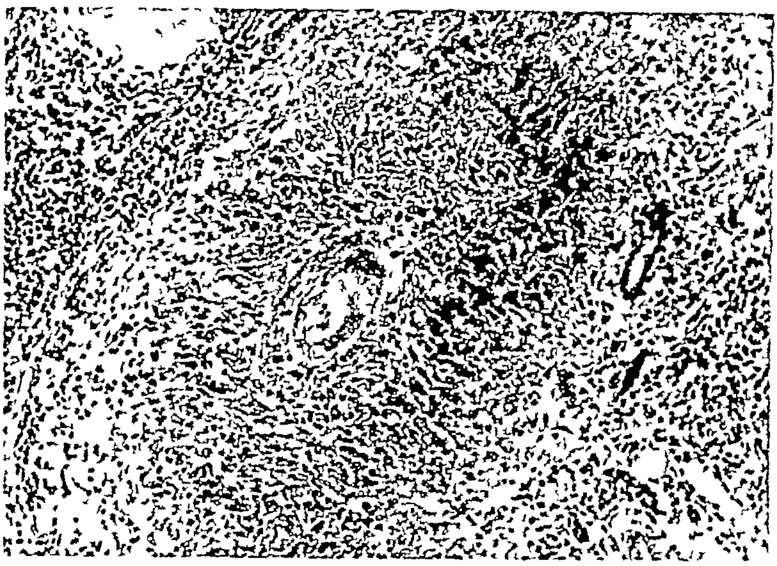


Fig 4—A small artery in the kidney showing fibrinoid change affecting the wall of the vessel and extending into the adjacent perivascular tissues There is minimal cellular reaction in the damaged area, possibly the result of suppression by cortisone. (Hæmatoxylin and eosin, ×40)

in the kidney does not exclude polyarteritis nodosa—a condition which may be confined to the vessels of one system

*Microdissection*—Representative portions from half of the kidney were taken through the cortex, medulla, and papillæ, and macerated in concentrated hydrochloric acid Some areas of the kidney showed obvious infarction, and it was found that the continuity of the nephrons in these areas had been destroyed and they could not be examined by this method

Many nephrons were dissected from non infarcted areas, they showed the following appearances

*Glomeruli*—The number of glomeruli did not appear to be abnormally reduced, and the majority were not obviously distorted

*Proximal tubules*—Examination of the proximal tubules including those with apparently normal glomeruli showed (1) patchy areas of translucency with localised areas of disorganisation, (2) all stages of necrosis with flattening of the epithelium, and (3) areas of epithelial regeneration with swelling and dilatation of the tubule (figs 6 and 7) Although the proximal tubules showed profound degenerative changes they did not appear to be unduly shortened nor was there evidence of compensatory hypertrophy, as seen in chronic nephritis The loops of Henle showed scattered areas of dilatation

*Distal and collecting tubules*—The distal and collecting tubules also showed profound degenerative changes with flattening of the epithelium, atrophy of the tubule, and dilation of the lumen, in other areas there was regeneration of the epithelium, and in some places continuous cast formation was observed (fig 8) The pathological changes were much more distinct in the collecting tubules than in the distal tubules

The most striking feature of the microdissection of noninfarcted areas was the extensive epithelial damage concentrated in the proximal and collecting tubules, while the glomeruli showed little distortion The changes in the proximal tubules were not unlike those previously described in the diuretic phase of acute tubular necrosis, and those in the collecting and distal tubules were similar to those described in a case of pitressin resistant diabetes insipidus (Roussak and Oleesky 1954)

## Discussion

Polyarteritis nodosa was not diagnosed clinically though a combination of hypertension, pyrexia, tachycardia, l increased erythrocyte sedimentation and some form of renal failure is, respectively, very suggestive The un nature of the renal failure was marked by a selective disturbance of tubular fun without severe impairment of glomerular function not having been described to our knowledge There are many manifestations of renal polyarteritis nodosa, which the commonest are proteinuria, hæmaturia, a rapidly rising blood-level, and, occasionally, oliguria associated pathological lesions con either necrotising arteritis with infarc or necrotising glomerulitis (Ahlstrom al 1953, Davson et al 1948, Ralston and Kvale 1949, Wainwright and D 1950), tubular changes in non infarcted areas appear to be limited to hydropic degeneration and some degree of stuffing with blood and casts in the lumina ( son et al 1948) In our patient, in unlike previously reported cases, there clinical evidence of severe tubular fa the histological appearances of the on section were similar to those pre reported The extent of the tubular became evident only *on microdissection*, and so it is *certain whether the tubular changes which* were th seen were out of the ordinary It is reasonable to supp that they were, because of the associated disturbance tubular function, but the question can be settled only by dissecting the kidneys in other cases of polyarteritis nodosa

Since the whole length of the tubules, including th collecting ducts, were abnormal it is not possible correlate precisely the structural with the functional abnormalities It is probable that the changes in th proximal tubules were responsible for the failure reabsorb solutes, and that the lesions in the collecting ducts were the cause of the hypotonicity of the urine its resistance to pitressin Large electrolyte losses after follow necrosis of the proximal tubules, as in acute tubular necrosis associated with abortion, &c (Oliv *1953), and pathological changes in the collecting tubules* have been described previously in cases excreti

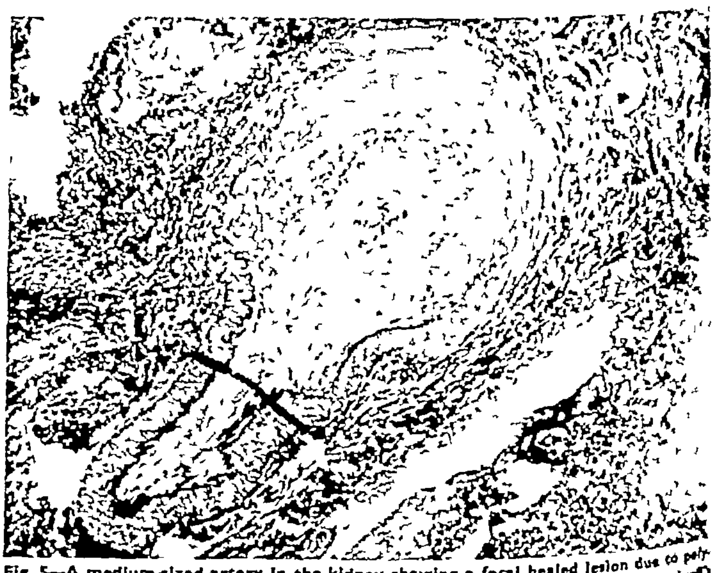


Fig 5—A medium-sized artery in the kidney showing a focal healed lesion due to polyarteritis nodosa. The internal elastic lamina shows segmental disruption. (Verhoeff's elastic stain, ×65)

ressin resistant hypotonic urine (Darmady 1954) The tive lack of structural change in the glomeruli in non infarcted areas is consistent with the normal od levels of urea and creatinine which were found, and h the small impairment of the glomerular filtration e.

he cause of the widespread tubular damage is obscure suggest that it was due to a similar mechanism to which produced the arterial lesions The ætiology of scattered glomerular lesions is more certain; the ent nature of many of the changes and the absence of widespread glomerular fibrosis is against their being equel to the attack of acute nephritis at the age of The possibility that the glomerular lesions were ated to the polyarteritis nodosa appears much more ly in view of the established association of a lomerulitis' with some cases of this disease (Davson al 1948, Grant 1940, Wainwright and Davson 0)

he development of tetany was of considerable interest began after a period of positive potassium balance and associated with a low plasma calcium The relatively ge and rapid decrease in plasma-calcium and the fact at the symptoms responded however temporarily, to intravenous administration of calcium indicate that change in the plasma-calcium level was probably the st important immediate cause of the tetany In a tassium-deficient subject, however potassium replace nt will sometimes induce tetany with only minor anges in plasma calcium concentration (Fourman 1954, ussak 1952) and it is possible that this mechanism s also present in our patient The clinical improve nt obtained by the administration of calcium however, ows that this was not the immediate cause, since tassium replacement tetany does not respond to lcium administration (Fourman 1954) Why the asma calcium should have fallen to the extent it did is t known; the excess urinary loss seems an unlikely use (Spencer et al 1952) In our patient the fall in asma-calcium followed a period of positive potassium lance and terminally after another period of negative tassium balance the plasma-calcium increased once ore to levels above normal We suggest that the rapid d extensive changes in potassium balance may have en responsible for the changes in the plasma-calcium

## Summary

A case of renal polyarteritis nodosa is described in hich the impairment of renal function consisted mainly tubular failure, shown by excessive urinary loss of ectrolytes and the excretion at all times of hypotonic ine uninfluenced by pitressin

At post mortem examination the kidneys were found have multiple infarcted areas and the characteristic ions of polyarteritis nodosa in the renal arteries; icrodissection of nephrons in the non infarcted areas owed widespread tubular damage and relatively intact lomeruli

We wish to thank Dr Evan Jones for allowing us to study e patient; Prof R J V Pulvertaft for the phase-contrast icrophotographs; and the Medical Research Council for expenses grant for the microdissection

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*References continued at foot of next column*

# TWO ATTACKS OF MENINGITIS WITH BRIEF INTERVAL

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IT must be very rare to have two attacks of meningitis due to different organisms at an interval of a month or so, as in the following case

A girl, aged 6 months, was admitted to the South Western Hospital on Nov 12 1953, with three days history of diarrhœa and vomiting

*In hospital* on Nov 16 she developed signs of raised intra cranial pressure: slight nuchal rigidity and tenseness of the anterior fontanelle

*Lumbar puncture* produced 5 ml of purulent cerebro-spinal fluid (C.S.F) under pressure Microscopy showed many polymorphs but no micro-organism. Meningococcal meningitis was provisionally diagnosed and intramuscular penicillin 500 000 units six hourly was given Culture of this specimen of C.S.F however gave no growth. The report on the C.S.F was as follows: turbid fluid containing 3200 leucocytes per c.mm. (lymphocytes 10% polymorphs 90%); a few red cells; no tubercle bacilli or other organism protein 100 mg per 100 ml globulin a trace, chlorides 660 mg per 100 ml sugar 44 mg per 100 ml

*Treatment and Progress.*—Penicillin treatment was con tinued and a course of Cremotresamide given in addition. On Nov 20 lumbar puncture was repeated and from the C.S.F a gram negative organism was isolated which proved to be *Hæmophilus influenzæ* On Nov 21 streptomycin 50 mg intrathecally and 500 mg. intramuscularly was given this was repeated daily until Nov 25 when lumbar puncture was discontinued Intramuscular streptomycin was given for a further two days. The child made an uninterrupted recovery and was discharged on Dec. 5 1953 The last specimen of C.S.F (Nov 25) gave no growth on culture

*Readmission.*—On Dec 14 nine days after discharge and nineteen days after the last lumbar puncture the child was readmitted with a return of the meningeal symptoms, and a relapse was presumed On lumbar puncture 2–3 ml of opalescent C.S.F was removed, and intrathecal and intra muscular streptomycin was given Microscopy, however showed pneumococci in large numbers in the C.S.F; and their identity was confirmed on culture The C.S.F was faintly opalescent and contained 178 white cells per c.mm. (lympho cytes 30% polymorphs 70%) Culture gave a heavy growth of pneumococci sensitive to all the antibiotics tried The C.S.F also contained protein 80 mg per 100 ml. some globulin chlorides 700 mg per 100 ml and sugar less than 15 mg per 100 ml.

*Treatment and Progress*—Chloramphenicol was started immediately and continued for eight days to a total dosage of 2 4 g Pneumococci were found in the C.S.F on two sub sequent occasions, but no growth was obtained on culture The patient's temperature did not subside immediately; so treatment was supplemented by a course of penicillin from Dec 22 until Jan 6 1954 The temperature fell to normal on Dec. 24 Thereafter the child made a good recovery and went home on Feb 10 She was seen again on May 20 when, except for a small boil in an axilla, she was in very good health On July 17 she developed whooping cough and was readmitted After a stay of seven weeks she returned home; a chest radiograph was normal and her general condition was very good

I am indebted to Dr R F L Hewlett for the laboratory investigations

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# CLOSTRIDIUM WELCHII EPSILON TOXIN IN THE INTESTINAL CONTENTS OF MAN

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The toxæmias of gas gangrene and acute obstruction of the small intestine have much in common In both conditions vomiting is frequent, the pulse rate raised, the blood pressure lowered, and the body temperature subnormal with coldness and cyanosis of the extremities, and some degree of general icterus commonly develops during the terminal stages , in both conditions the mind is alert, often abnormally so, and consciousness is usually retained to the end , and in both conditions anaerobic bacilli capable of producing lethal toxins are to be found in large numbers at the site of disease

Williams (1926, 1927) presented some evidence in support of the hypothesis that the toxæmia of acute intestinal obstruction was due to the absorption of the toxins of *Clostridium welchii* from the contents of the obstructed intestine, and he claimed a substantial reduction in mortality through the use of *Cl welchii* antitoxin in the treatment of this and allied conditions Other workers, however, were unable at that time to confirm that the toxicity of the intestinal contents of experimentally obstructed animals was due to any specific bacterial toxin , this work has been fully reviewed by Oakley (1943)

Since then improvements in the methods used for the isolation and identification of the clostridia and their toxins has led to the recognition of the important part played by some of these toxins in the production of a far wider range of disease in man and animals than had been suspected hitherto For example, lamb dysentery *and enterotoxæmia of sheep, and* gas gangrene, enteritis necroticans, and a mild type of food-poisoning in man are now all attributed, in whole or in part, to the toxins of *Cl welchii*

The similarity between some of the clinical features of enterotoxæmia of sheep and severe cases of acute intestinal obstruction in man, coupled with the predominance of *Cl welchii* in the lesions of both conditions, suggested to us that the toxins of *Cl welchii* might after all play some part in the production of toxæmia in intestinal obstruction The demonstration of *Cl welchii* epsilon toxin in the intestinal contents of the following fatal case of acute obstruction of the small intestine supports this contention

## Case-record

### *Clinical*

A flour screener, aged 53, was admitted to Addenbrooke s Hospital on Jan 5, 1954, with a twenty four hour history of severe colicky, central abdominal pain accompanied by frequent vomiting of small amounts of thin brownish fluid He had been constipated for the previous two days and had passed no flatus since the onset of pain He had been successfully operated on for a strangulated inguinal hernia nine years before

*On admission* he was pale, shocked and in obvious pain, with temperature 97°F, pulse rate 120, *and blood pressure* 130/85 mm Hg His abdomen was slightly tender , bowel sounds were absent and radiography of the abdomen showed fluid levels in the small intestine

*At operation* free bloodstained fluid was found in the peritoneal cavity together with five feet of gangrenous ileum strangulated by an omental adhesion to the base of the mesentery The gangrenous intestine was resected and continuity restored with an end to-end anastomosis A pint of dextran was given intravenously during the operation and glucose saline solution on the patient s return to the ward

His general condition from the time of admission poor, and about five hours after the operation he suddenly, with a pulse rate of 140 and a systol pressure of 60 mm Hg Although further dextran was given, together with intravenous noradrenaline methedrine, his pulse rate and blood pressure unchanged, *and he died three hours later*

*Necropsy* —The anastomosis was intact, and the above and below it appeared to be healthy Near the mosis there was a thrombus bulging from a small the superior mesenteric artery, about 2 mm in di *there was about 2½ litres of bloodstained* fluid and b in the peritoneal cavity, the latter mainly in the neigh of the anastomosis The ileum and colon contained 250–300 ml of heavily bloodstained liquid fæcal m Apart from evidence of benign hypertension and a small of the liver, no other abnormalities were found

### *Bacteriological Investigations*

Samples of intestinal contents were taken from ileum just above the site of resection and from the immediately below the ileocæcal valve Both spe were heavily bloodstained and contained a very number of organisms, a great many of which had typical appearance of *Cl welchii*

A portion of each specimen was mixed thoro with an equal amount of 0 9% saline solution and fuged at about 5000 r p m for thirty minutes intravenous injection of 0 4 ml amounts of the supernatant fluid of either specimen killed in thre four hours mice weighing 20–25 g This amount of material was neutralised by 0 1 ml of a *Cl welchii* ty antiserum but not by 0 1 ml of a *Cl welchii* ty antiserum As the type D antiserum contained 23 al units and 310 epsilon units per ml and the type antiserum 155 alpha units and <0 01 epsilon units ml , it was considered that the lethal agent for mice the intestinal contents from this case was *Cl* we epsilon toxin

A rough titration showed that both samples of in tinal contents contained about 20 mouse M.L.D gramme, from which it was calculated that there was least 5000 mouse M L D of epsilon toxin in the intes contents at the time of the necropsy

A portion of each sample of intestinal content inoculated into 1 oz bottles containing 10% pap digest broth and meat particles After eighteen ho incubation at 37°C both these mixed cultures conta epsilon toxin

Both the original material and the mixed cultures g heavy growths of *Cl welchii* on 10% horse blood plates Most of the colonies of *Cl welchii* on these pl were rough and crenated In broth culture these prod no toxins lethal to mice except alpha and were there assumed to be *Cl welchii* type A A few colonies, howev were smooth and round, and in broth culture these pr duced alpha and epsilon toxin but no beta or iota tox This was considered characteristic of *Cl welchii* type

## Discussion

*Clostridium welchii* type D is found in large numbers the intestinal contents of sheep dying from enter toxæmia, and the absorption of the epsilon toxin produced by this organism is generally believed to be the immedia cause of death

The present case of acute obstruction of the sma intestine provides evidence that the epsilon toxin *Cl welchii can also be found in the intestinal tract of man*

Before any importance can be attached to the presence of a bacterial toxin in a necropsy sample of intestin contents, it is obviously essential to exclude the poss bility that the toxin has been produced by the intestin flora after death

Samples of the contents of the ileum were taken duri the necropsy of 33 cases selected at random from a variety of conditions, and these were examined for the presence of toxins by intravenous inoculation into mice Although *Cl welchii* was isolated with ease from on f these specimens there was never any evidence of presence in any of them of toxins lethal to mice urthermore in the present case the body was placed the *mortuary refrigerator within two hours of death,* it remained there until the necropsy about forty ht hours later the bodies of the 33 controls were also red under the same conditions

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* I of a grant from the Agricultural Research Council

It therefore seems reasonable to postulate that in the ent fatal case of acute intestinal obstruction *welchii* type D was present in the small intestine at the te of obstruction and that a considerable amount of ilon toxin was produced during the enormous and *ild proliferation of the intestinal flora that takes place* such occasions

Although the immediate cause of death was probably udden postoperative hæmorrhage the patient s poor eral condition before and during the operation may ve been partly due to the absorption of epsilon toxin m the obstructed intestine

## Summary

The presence of *Clostridium welchii* epsilon toxin in the isolation of *Cl welchii* type D from the intestinal *ntents of a fatal case of acute obstruction of the small* estine are described and discussed

We wish to thank Mr P H R Ghey for access to the ical notes of this case; Mr W Sewell for drawing our ention to it in the first place; Dr G A Gresham for the cropsy findings Dr A M Barrett and staff for help in the lection of the control samples of necropsy intestinal con nts and Mrs Irene Batty of the Wellcome Research oratories, for details of the sera used in the neutralisation ts

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# RECOVERY OF CLOSTRIDIUM WELCHII TYPE D FROM MAN

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ORGANISMS of the *Clostridium welchii* group type A lobbs et al 1953 Beck et al 1954) and type F (Zeissler d Rassfeld Sternberg 1949 Oakley 1949 Hain 1949) ve repeatedly been *isolated* from cases of food poisoning d there is little doubt about their pathogenicity pe D however has not so far as we know been und before in man *That it* may cause intestinal sturbance in man is shown by the case reported here

## Case report

A male shoe repairer aged 41 with a history of amœbic entery treated in 1943 followed by mild postdysenteric litis, was admitted to hospital for treatment of long anding ankylosing spondylitis. During his stay in hospital e suddenly developed violent attacks of diarrhœa, passing 14–18 stools in twenty four hours. Defæcation was always ceded by abdominal pain which subsided after passage of the stool. The stools were liquid and yellowish brown contained mucus and pus, had no offensive smell and only very *occasion* ally showed small specks of blood Microscopy of the fæces showed fairly numerous leucocytes scanty red blood-cells, and flagellate *Trichomonas hominis* There was no vomiting d no dehydration and no pyrexia and the patient s general condition was remarkably good

*On examination* his abdomen was soft and not tender on palpation; his liver and spleen and respiratory cardio-vascular and nervous systems were normal; and his blood and urine were *normal* A barium enema showed only a slight diminution of haustration distally At first the condition was thought to be *only* an exacerbation of his old postdysenteric colitis but the rather violent bowel symptoms suggested the possibility of food poisoning and the stools were sent for bacteriological examination.

*Bacteriological Findings*.—Routine examinations for organ isms of the salmonella and shigella groups and for staphylococci were negative A direct gram-stained smear revealed many rod shaped gram positive spore bearing organisms morpho logically resembling clostridia Anaerobic culture on horse blood agar yielded a profuse growth of smooth and slightly convex colonies about 2 mm in diameter with a large zone of hæmolysis which, on first isolation had an irregular fimbriated edge On subculture these colonies became round with an entire edge, and had the characteristic appearance of *Cl welchii* The organism was Nagler positive and liquefied gelatin A culture was sent to Dr Betty Hobbs at the Colindale Public Health Laboratories for final identifica tion and typing The organism was identified as *Cl welchii* but on serological examination did not agglutinate with either antisera prepared from *Cl welchii* isolated from cases of food poisoning or with type-F antisera.

## *Toxicology*

A filtrate from the strain of *Cl welchii* grown in 1% glucose broth for five hours was sent to one of us (G H W) by Dr Hobbs The filtrate was examined for toxigenicity by the methods described by Oakley and Warrack (1953) and the following *Cl welchii toxins* were detected α ε θ κ and ν There was no trace of β δ, ι, λ and μ This toxigenic pattern is consistent with *that expected from a* type D strain The strain was *also* grown in meat broth medium for five hours and a similar toxigenic pattern was found in the filtrate

In view of these findings the patient's fæces were re-examined four weeks later, and again a *pure culture* of *Cl welchii* was isolated Culture filtrates from this strain grown for five hours in meat broth *medium gave* exactly the same results as the original strain

The patient was bled *four* weeks after the onset of illness and his serum was found to contain 0 2 unit ε antitoxin per ml whereas the sera from nine healthy controls contained no detectable ε antitoxin (< 0·01 unit of ε per ml )

## Discussion

*Cl welchii* type D is often recovered from cases of enterotoxæmia in sheep and goats but is also found in the intestine of healthy animals of these species Borthwick (1937) found type D in the intestines *of three* guineapigs and two dogs Taylor and Gordon (1940) in the intestines of two cattle, one sheep and seven rabbits and Bullen (1952) in forty-six of a hundred sheep

Since *Cl welchii* type D *occurs* in the intestinal tract of healthy sheep it is suggested that some alterations *must* take place in the healthy environment before the organism can multiply rapidly and produce toxin (Bennetts 1932, Roberts 1938 Bullen et al 1953)

The problem of the pathogenicity of the *strain of Cl welchii* type D isolated in the present case is somewhat complicated by the history of postdysenteric colitis. This condition may however have been the predisposing factor creating a favourable *environment* for infection with the organism The facts that *Cl welchii* type D was again isolated *after an interval* of four weeks and that the titre of the patients serum was 0·2 *unit* ε anti toxin per ml , *suggest* the presence of an infection which may have been responsible for the recent bowel symptoms *or at least stirred* up a dormant condition

We thank Dr Betty Hobbs and Dr M *Sterne for* providing the culture filtrates and Mrs I Batty for determining the ε antitoxin

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### A NOTE ON

# OSTEOSCLEROTIC CHANGES DUE TO CHRONIC INFECTION OR NEOPLASIC INFILTRATION

## SECONDARY (NEOPLASIC) MARBLE BONES

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Cases of chronic osteoperiostitis due to congenital (inherited) syphilis in children, leading to deformities of the lower extremities (the tibiæ being especially affected) somewhat resembling osteitis deformans in adults (Paget's disease of bones) are fairly well known The resulting clinical picture may be extremely grotesque, when the chronic inflammatory process leads to great increase in the length of the legs (Weber 1908) Here one ought to refer to the occasional well-known connection of Paget's bone disease with true neoplasia, as illustrated in my paper with H Huber on Osteitis Deformans (Weber and Huber 1939) in a group of three elderly sisters with *osteitis deformans*, one of them aged 66 developed spindle cell sarcoma in the affected skull

F Reiche of Hamburg (1929), in his account of "osteo sclerosis generalisata fragilis," very carefully described a case of a professional man, who died in 1927 in his 49th year with a condition resembling the "marble bone" disease of Albers Schonberg, dating from his quite early life, or birth, and almost certainly ætiologically connected with congenital (inherited) syphilis I lay great stress on Reiche's account, because it appears to have been the original, or one of the original cases on which Albers-Schonberg himself founded his description of the marble bone disease Albers Schonberg saw the patient in 1904 and published skiagrams of the bones I may mention that I heard of this case from Reiche himself whom I knew personally , he had been resident house-physician at the German Hospital, London, before my time

My colleague, Dr E Schwarz, allowed me to report a most interesting case under his care in the German Hospital, London, in which the symptoms were most confusing At first I thought that malignant neoplasm could be excluded, but owing to the kind assistance of Prof Harvey Cushing in America, I found that the case was certainly one of metastatic carcinomatosis from a primary cancer of the prostate (Weber 1929) The prostate was not enlarged though hard The whole bony skeleton was involved It seemed as if the cancerous prostate had been pouring all its cancer cells into the circulatory blood, whence they were caught up by all parts of the bony skeleton There they produced new bone formation, in some parts actually converting the cancellous tissue into solid bone The periosteum was also involved in the formation of new bone, and the dura mater lining the cranium was affected as if it represented the periosteum of the inner aspect of the calvarium Thus, specimens given to the Royal College of Surgeons were described in the catalogue of the pathological collection as follows

*S 78 4 —Calvarium Metastasis from prostatic carcinoma*
From a man aged 56 who died with carcinoma of the prostate and widespread diffuse bony metastases

Specimen Part of the left side of the calvarium showing several thin irregular deposits of new growth on the inner surface The cut edge shows that the diploe has been obliterated by dense bone

*N 11 1 —Dura Mater Metastasis from prostatic carcinoma*
Specimen A portion of the dura mater from the vault of the skull The inner surface is studded with nodules of new growth up to half an inch in diameter

Many thousands of unicellular carcinomatous meta[illegible]st have been required to produce this infiltration of the skeleton, and this would account for the [illegible] of the cancerous prostate Why the soft parts of the should not also be involved is of course an question, but may be compared to the fact that other neoplastic metastatic infiltrations are confined special portions of the body compare the metastases in the Robert Hutchison type of neuroblastoma or sarcoma in children, and also metastatic inflammatory infiltrations—e g , meta abscesses confined to the bony skeleton in some cases of typhoid fever

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# Preliminary Communication

## MELANOPHORE-EXPANDING ACTIVITY HUMAN PITUITARY GLAND

During the past three years there has been siderable discussion about the relationship corticotrophin and melanophore expanding (M E H ) Some workers claim that the pig turbance in patients with Addison's disease results excessive secretion of M E H by the pituitary g With this hypothesis we are in general agreement

Reasonable proof of this hypothesis depends on demonstration not only of increased melanoph expanding activity in the blood of such patients but of similar activity in human pituitary tissue So far we are aware, the presence of M E H in human pitu tissue has not previously been reported We report *the presence of a substance with melanophore-expan activity in the human pituitary gland*

*Fresh human pituitary tissue* was obtained from woman, aged 52, who had undergone hypophysect for advanced metastatic malignant disease (pri breast carcinoma) The pituitary gland was rem piecemeal and placed immediately in cold absolute tone A powder was subsequently prepared by conti extraction for three hours with acetone and drying concentrated sulphuric acid This dried powder we 53 4 mg

*This powder was next extracted for thirty minut* 70°C in 3 ml of glacial acetic acid After filtration extract was diluted so that the normality of the solution as regards acetic acid was 0 1 The pH adjusted to 4 0, and 120 mg of oxycellulose pow (12% COOH) was added. After being stirred continu for forty-eight hours the oxycellulose was collected shaken with 2 0 ml of 0 1 *N* HCl for sixteen hours. eluate was *collected and neutralised* and the solu assayed by injection into intact male *Xenopus l* toads The degree of melanophore expansion was m ured at ninety minutes A self contained four p assay was done, the test material being assayed again substandard powder with melanophore expanding ac vity (corticotrophin, Commonwealth Serum *Labo* tories, batch P 60)

This assay showed that on a weight-for weight bas this substandard powder possessed 83 times the pote of the crude human powder, with fiducial limits of and 100

We are of the opinion that this observation provi additional information on the possible mechanism of the pigmentary disturbance observed in patients Addison's disease

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# Reviews of Books

### nistry of Lipids of Biochemical Significance

I A. LOVERN London Methuen New York: John Wiley 1955 Pp 132 8s 6d

his monograph is a worthy successor to the previous in the same series by Smedley Maclean, which ared twelve years ago Four of the five chapters ased upon a series of lectures given at the University berdeen the fifth (on the preparation and analysis ids), added since, is a valuable companion to them

e author deals first with the structure of lipids as isolated then with their physicochemical relations to the cell ana. One chapter is devoted to the intermediary meta- n and dynamic turnover of the lipids in vivo as revealed be use of labelled isotopes, and the concluding chapter with lipid function This chapter is short and many wish that more space had been devoted to the function ids in relation to cell structure and metabolism and less eir preparation and analysis The term lipids includes terols, triglycerides, and glycerophosphatides and the group embraces a bewildering range of chemical com ds containing amino-acids, amines, aldehyde derivatives, hydrates, inositol and other substances so the author attempted to compress a great deal of information within y small compass.

e has been successful in that he has produced a very able and informative book with a sufficiency of tural formulæ to allow anyone with a basic know e of biochemistry to understand it. It will be just thing for advanced students and lecturers whose ialty does not lie in this field and it may also appeal e inner circle of lipoid chemists. References to the nal publications are plentiful but not exhaustive.

### rnational Review of Cytology

ol. III Editors G H BOURNE London Hospital Medical College and J F DANIELLI zoology depart ment King's College London New York Academic Press. 1954 Pp 530 $9 50

YTOLOGY is here taken to include physiological as as morphological studies at the cellular level and editors have ranged widely in their choice of ributors.

Waymouth shows how the exponents of tissue-culture nique like their microbiological colleagues are moving from complex media of uncertain composition to syn le media susceptible of precise chemical definition. It s that metazoan cells can now be kept alive in totally etic media for up to 70 days, though not without some ution in viable-cell count O Bucher appraises statis lly the practicability of measuring volume-change in ear populations and I Cornman follows him with a short admittedly discursive account of what is known about cellular pharmacology of urethane M Alfert in plendidly illustrated article considers the nature of the t chromosomes, and R A Beatty deals with inconstancy chromosome-number in the somatic cells of mammals. o specially topical reviews deal with the biochemical racteristics of cellular inclusions: A. L. Dounce covers metabolic activities of isolated nuclei with which he worked extensively and C de Duve and J Berthet give outstandingly good account of the application of differential rifugation to the separation of cellular components Gustafson contributes a detailed essay on the inhibitory ect of lithium on the respiratory activity of that favourite chemical embryologists the sea urchin's egg In reviewing histochemical applications of the azo dyes Everson Pearse phasizes a number of guiding principles for histochemical ctice generally R. G Williams gives a useful summary of scope of techniques employing transparent chambers in bit ears and elsewhere G Asboe Hansen writes on the mast ll, and E. W Dempsey and A I Lansing give a commend ly brief report on what little is known about the molecular ucture of elastic tissue In a final paper S O Brattgard H. Hyden discuss microchemical studies of single nerve- lls and the extension of microspectrophotometry from the re familiar ultraviolet region to that of the softer X rays. he papers go rather deeply into this great variety of ds but (in addition to professional cytologists) experimental pathologists and others with biochemical and histological leanings will find much profitable reading in them

### Babcock's Principles and Practice of Surgery

2nd ed Editor KARL O JONAS M D M.S F.A.C.S F I C.S instructor in surgery Temple University School of Medicine Philadelphia. London: Henry Kimpton 1954 Pp 1543 £6 15s

Ten years ago Dr W W Babcock's *Textbook of Surgery* was expanded, with the aid of thirty-seven collaborators, into the *Principles and Practice of Surgery* It then represented mainly the teaching at Temple University, Philadelphia. Many of the fifty four contributors to this new edition practise and teach in Philadelphia, but it is an eclectic work. Dr Jonas, as editor, has allowed his team to present uncommon conditions together with the common in an endeavour to produce a comprehensive volume

In some subjects the consequent condensation has led to tabulation, particularly in the urological section The thoracic, orthopædic and neurosurgical specialties are fully considered while pædiatric surgery has gained a section to itself Gynæcology is omitted and so is otorhinolaryngology though descriptions of many of the conditions and procedures asso ciated with this specialty are scattered through the sections. As a result of these gaps conditions such as ectopic pregnancy and otitis media are not described. But the work is in parts broad in conception and even original for there is a general chapter on surgery during pregnancy preceded by another on surgery and diabetes while the last chapter not only describes the mental state of the surgical patient but also contains some shrewd observations from a psychiatrist on the personality of a surgeon. For English taste the section on anæsthesia is perhaps overweighted with spinal and regional methods. Irradiation therapy is mentioned only cursorily and the lack of a detailed account of radioactive isotopes and their uses is surprising The description of Trendelenburg's test for varicose veins is mystifying Illus trations are profuse many are good some indifferent while the few colour plates are poor

Any textbook with this ambitious scope must have weaknesses and in this work their number is not excessive The cost of the book matches its weight.

### The Vitamins

*Chemistry Physiology Pathology* Vol III Editors W H. SEBRELL, jun director National Institutes of Health Bethesda, Maryland; ROBERT S HARRIS professor of biochemistry of nutrition Massachusetts Institute of Technology Cambridge New York: Academic Press. London: Academic Books. 1954 Pp 605 $15 00

THE third and final volume in this new series of reference works on the vitamins deals in turn with *p*-aminobenzoic acid, pteroylglutamic acid, vitamin $B_6$ riboflavine aneurine, the tocopherols, and miscellaneous growth factors such as lipoic acid and carnitine As in earlier volumes, each section on each vitamin has been written by an expert on the particular subject. Up till now most books about the vitamins either have dealt exhaustively with one vitamin or group of vitamins or have surveyed the whole field generally The present series, by giving a full and up to-date account of all the vitamins, is a welcome addition Even in a work of this size not all relevant information can be included but the editors and contributors have succeeded in incorpor ating all the main findings. Numerous references are given to original papers, and each volume is well provided with tables and illustrations.

### Maxillofacial Anatomy

HARRY H. SHAPIRO D.M D., assistant professor of ana tomy College of Physicians and Surgeons, Columbia University Philadelphia J B Lippincott London: Pitman Medical Publishing Co 1954 Pp 302 96s

THIS textbook is partly based on a smaller volume, *Applied Anatomy of the Head and Neck*, which Dr Shapiro wrote eleven years ago. As the work of an anatomist and surgeon mainly concerned with dental and oral surgery its main appeal is likely to be to dental surgeons, but it offers an original and clear approach to the complex anatomy of the facial skeleton and neighbouring tissues

The drawings are admirable, and many illustrate unusual but important aspects which are rare in conventional textbooks of anatomy Photographs and radiographs are also clear and helpful The text is designed on a morphological rather than a regional basis, so the student may not always find it easy to form a composite picture of bony, vascular, neural, and muscular elements Dr Shapiro has also added "practical applications" of anatomy, to show its usefulness in practice, but these digressions are sometimes unworthy of the rest of the book It is not helpful to discuss burns in four hundred words or cleft lip in two pages Some of the surgical techniques advocated are unlikely to win general approval

The book is beautifully produced and is a pleasure to handle as well as to peruse

### Medicine, Magic and Mythology

Dr John Precope London Heinemann Medical Books 1954 Pp 284 42*s*

This is an account of the evolution of pre-Hippocratic medicine based on the study of anthropology and a knowledge of Ancient Greek. In it the author traces the development in men's minds of, first, the appreciation that disease as an entity exists and should be combated, then that it can be cured by magic, and then that it can be cured by magic aided by material things such as plant and animal extracts After this came the faint beginnings of experimental medicine, sometimes aided, sometimes retarded, by the new systematised tales of mag mythological tales that are the wonder and glor Greek mind The text is broken up by numerous tions in Greek (usually with an English trans which make it rather difficult to read But it will students of prehistoric medicine, especially if are anxious to brush up their Greek at the same

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**Textbook of Gynæcology** (9th ed London A Black. 1954 Pp 493 40*s*)—After three and a h Prof James Young's textbook is substantially th but advances in our knowledge of endocrinology, dis menstruation, prolapse of the uterus, and uterine and tumours all find a place in the new edition. The printer some of the illustrations, are beginning to look a tr world, and a few of the photographs are too vague to serve their purpose

**Physical Signs in Clinical Surgery** (12th ed John Wright & Sons 1954 Pp 456 38*s* 6*d*)—In th going days of 1949 this book appeared in four paper parts, but now it is back between comely boards Hamilton Bailey has this time had the help of Mr Clain, who has rearranged the text so as to include tive chapter on the orbit, and has combined the ch the spine and the sacro iliac joints—structures which are not easy to consider apart Mr Bailey himself h salt on the tails of some supplementary physical sign had escaped him till now, and caged them in a final The illustrations are as good as ever—every one of clinical demonstration

# New Inventions

## A CONSTANT INFUSION APPARATUS

Many methods used today in clinical medicine—e g, in the estimation of renal clearance and of inulin space—require an apparatus capable of delivering fluids at a constant rate Most of these methods are based on the principle of a geared-down electric motor driving the piston of a syringe forwards into the syringe barrel[1] These methods have several disadvantages, the initial expense of the apparatus, the variation of motor speed with voltage changes in the mains electricity-supply, and the errors involved if it is necessary to refill the syringe during an infusion

The apparatus described here is a modification of a simple blood-transfusion unit It has a capacity of 250 ml (or larger if required), needs no motor, and is inexpensive It can be sterilised easily and is transportable It is particularly useful where the mains electricity-supply is either non-existent or of poor voltage stability, it has been successfully used in a recent investigation in East Africa[2]

RATE OF FLOW OBTAINED DURING ESTIMATION OF SUCROSE SPACE IN A PATIENT WITH ASCITES USING APPARATUS DESCRIBED

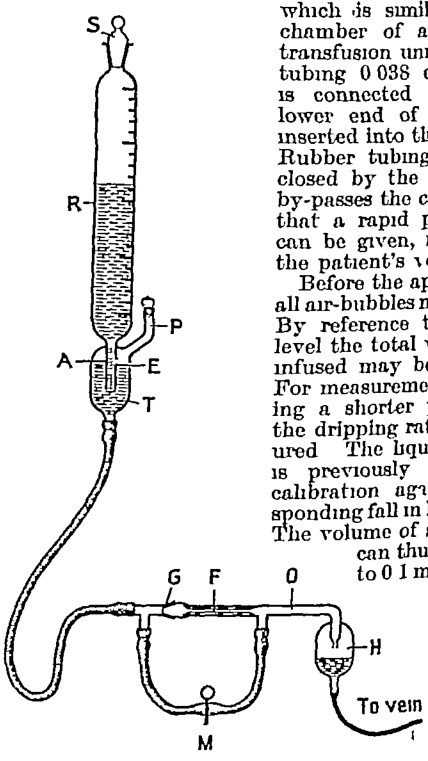
| Period of infusion (min) | Rate (ml per min) |
|---|---|
| 0–125 | 0 77 |
| 126–155 | 0 77 |
| 156–184 | 0 79 |
| 185–244 | 0 79 |
| 245–274 | 0 78 |

A constant head of liquid is maintained above a glass capillary tube For a capillary tube of a given diameter the flow will depend on the head of liquid above the tube, and this is varied according to the flow required

In our apparatus (see figure) the reservoir (R) consists of a tube (32 × 4 cm) of uniform bore and with a capacity of 250 ml It is graduated at 2-ml intervals A ground-glass stopper (S) closes the reservoir at the top The lower end of R leads into a constant-head device (T) which maintains the liquid at the level E At E a hole (diameter 0 5 cm) is blown into the side of a tube (A) 0 5 cm in diameter leading from R P a side-arm open to the atmosphere, has a small sterile cotton-wool plug placed in its mouth

The lower end of T is joined by flexible tubing to the ground-glass joint (G), the cone of which bears the capillary tube (F) F has an internal diameter of 0 047 mm (about the size of the stylet of a needle) The capillary tube need only be appro of this size The capillary tube widens out into a (O) of bore 0 3 cm, and this is sealed into the ch which is similar to the chamber of a normal transfusion unit 'Polyth tubing 0 038 cm in is connected to the lower end of H and ca inserted into the patient's Rubber tubing, which closed by the gate-clamp by-passes the capillary that a rapid priming can be given, if required the patient's vein

Before the apparatus is all air-bubbles must be remo By reference to the level the total volume of infused may be read to For measurements of flow ing a shorter period of the dripping rate in H is m ured The liquid drop vo is previously determined calibration against the c sponding fall in liquid level The volume of solution inf can thus be determ to 0 1 ml In practice has been fo advisable use hepar ised solution The appro mate rate infusion required is tained be the polythene tubing is in the patient's vein The tube is then inserted, and the height of E above the capillary tube F is adjusted until the required rate is obtained.



We wish to thank Mr J H Burrow, B.Sc, for his inter and technical skill in making the prototypes of this appar

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[1] E g Last C F *Brit med J* 1945 i 122

[2] [illegible] H and Schnieden, H Unpublished observations

# THE LANCET

*LONDON SATURDAY, FEB 19 1955*

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## Money for Hospitals

ough little change can now be made in the small amme of capital works for our hospitals in -56 the two following years are to see a rise in nditure—and none too soon For the "replace t or redeployment of worn out, obsolete or iciently disposed plant" hospitals in England and es are to have £2 million in 1956–57 and £4 million 957–58, and in the latter year the total expendi on building and plant is likely to reach £18 ion. In Scotland the total provision for hospital ding is to be increased from £1·0 million this year 2·5 million in 1957–58 In his statement to the se of Commons last week the MINISTER OF HEALTH lained that the English hospitals have already nced a first batch of major projects to a total ue of £7 million, and these will almost certainly among those started under the new policy They ude new general hospitals or the first stages reof, for Welwyn, West Cumberland, West Corn l, Harlow, and Swindon a new mental hospital Wolverhampton several big extensions to ting mental-deficiency hospitals, and half a en extensions, mainly to outpatient departments various parts of the country Mr MACLEOD also ted that in a few years' time work may begin on ew teaching hospital at Cardiff the rebuilding of ring Cross Hospital at Harrow (which may or y not get into the 1957–58 programme), and the ition of a new ward block to Guy's

This loosening of the Treasury purse strings is ted welcome, but the plans now outlined must ertheless be seen in relation to the needs of hospitals seven years after their transfer to the ional Health Service Like the roads and the ways they have been allowed no major development and only working maintenance for over fifteen rs During this period of rapid medical progress and ing demands from the public capital expenditure hospitals in England and Wales has been only out £7–9 million a year—a sum considerably below hat is required to cover normal depreciation. The ere need to replace worn-out boilers has proved a major strain on the small budgets for improvements n the regional hospitals as the recent experience of St. George's Hospital at Ilford plainly illustrates[1] A year ago it seems, the *management committee* of this hospital issued a warning that its boilers were worn out and when these failed during the cold spell last month the work of the wards and operating theatres was kept going only with great difficulty Two new boilers had in fact been delivered six months previously, but owing to previous cuts in capital expenditure building of the new boiler house which was to house them had been postponed to 1959 Some idea of the inadequacy of the present allowance for capital works can be gained by recalling that the Middlesex County Council before the war was spending £500,000 a year on improving its hospitals, without building any new ones Mr JOHN FREMANTLE, chairman of the North West Metropolitan Regional Hospital Board, has lately pointed out that this modest pre-war programme cost the county council proportionately five or six times as much as is now being spent on similar work in the board's far larger region

During the brisk interchange in the House of Commons following his announcement, Mr MACLEOD mentioned the circular[2] in which his Ministry has indicated various ways in which improvement of plant can reduce the cost of engineering kitchen, and laundry services The list is a useful one, but it does not contain some equally urgent items of the kind that lead to savings in a less direct way For example nothing is said about the very real need in many hospitals to raise the level of kitchen hygiene It is an unfortunate fact that the lavatory and wash basin accommodation for hospital kitchen staff often falls far short of the standards now normal in industrial catering establishments, episodes of food poisoning are commoner than they should be and backwardness in this respect is wasteful as well as being particularly improper in a medical institution And let nobody suppose that the improvements badly needed in our hospitals for the achievement of running efficiency, are only in things like heating systems and laundry plant, for in very many places the basic requirements of clinical medicine still have to be fulfilled All too often outpatient departments and ancillary services are insufficient, wards are overcrowded and the staff work at a disadvantage because they lack elementary facilities An extra million pounds in a couple of years' time can make only a small impression on the country as a whole the Sheffield regional board alone has plans for small scale improvements totalling £2 million. On the other hand we can rejoice at least that the period of unexpected cuts has, temporarily at any rate, come to an end, and that a forward step has been found possible We can rejoice too at what amounts to the introduction of planning over a three-year period Above all the Minister's statement will be welcomed for its promise of new hospitals as well as the renovation of old ones Here again the need is undoubted for up till now no attempt has been made to match hospital facilities to changing populations and no policy has been formulated for the regular replacement of worn out buildings We must hope that it will not be long before he is able to give us an idea of principles to be followed and a policy to be pursued Since the war there has been a great influx of postgraduate students to this country, and in the hope that Great Britain may be able to hold its position as a world medical centre, one would like to see a policy adopted by which most of the teaching centres could be rebuilt in the next thirty years But this is of course only one of the problems—many of them exciting—that will arise when, so far as the hospitals are concerned, the late war can be regarded as over

In his statement the Minister referred to the possibility that some hospital building work would be financed from other sources—i e , from endowments and free moneys These funds are very unevenly distributed, but even in small amounts they have proved invaluable to many hospitals The Willesden General Hospital in north-west London is shortly opening a much-needed extension of the pathological laboratory, provided entirely from private funds At this busy hospital, outpatient work is still being done in a cramped and unsatisfactory corrugated-iron building erected as a temporary measure during the first world war In the past seven years many hospitals have had reason to be grateful to the medical foundations, particularly the King's Fund, which, in the Metropolitan area alone, in five years contributed £108,000 towards new kitchen equipment, in addition to many other services and grants Nobody wants to return to flag-days , but it has become increasingly clear that a hospital, like a university, can often make excellent use of free moneys, and also that the public still has a great regard for the hospitals and is not unwilling to give them money, provided this does not go into the bottomless Treasury pit They would get far more support of this kind if their needs were better known In the old days, the voluntary hospitals had ample publicity, and the local-authority hospitals were controlled by elected representatives of the public, who could press for a better service Today hospitals are rightly debarred from direct financial appeals to the public, but there are still many good reasons for maintaining or restoring local interest and pride in their work People should feel that the hospital which serves them is *their* hospital, and if this feeling makes them want to do something special for it, let us be thankful for the help

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[1] *Ilford Recorder* Feb 3

[2] Circular H.M.(55)19

## Cl Welchii as Intestinal Pathogen

ON earlier pages of this issue two groups of workers independently report the isolation for the first time of *Clostridium welchii* type D from lesions of the intestine in man These reports complete an interesting circle which began in 1926 when WILLIAMS[1,2] described evidence which in his opinion suggested that the toxæmia of acute intestinal obstruction in man was due to the absorption of the toxins of *Cl welchii* from the contents of the obstructed intestine Unfortunately, the greater part of the clinical evidence was indirect, in that it rested on the benefits that apparently resulted from treating intestinal obstruction and allied conditions with gas-gangrene antitoxin The experimental evidence rested mainly on observations on dogs—animals whose organs and tissues often contain *Cl welchii* in large numbers Thus it was uncertain what conclusions applicable to man might be inferred from the good effects which WILLIAMS noted after giving gas gangrene antitoxin to dogs in which he had produced obstruction of the intestine In general, WILLIAMS's medical colleagues accepted his evidence that *Cl welchii* grew abundantly within loops of intestine proximal to an obstruction, but they were unable to confirm that the associated toxæmia was due to toxins produced by the organism By a fortunate chance WILLIAMS's work came to the notice of BENNETTS, a veterinary surgeon in Western Australia, at a time when he was preoccupied with enterotoxæmia in sheep BENNETTS found *Cl welchii* in great numbers in the intestine of sheep w disorder,[3] and—more important—he found tha intestinal contents of affected animals and c filtrates of the clostridium both contained a t *Cl welchii*, now designated ε toxin, whi absorbed into the blood-stream It is u established that *Cl welchii* type D—the c found by BENNETTS—is an important in pathogen of sheep In man *Cl welchii* type A i known as the most important of the gas- organisms It has been found to be one o mild food-poisoning,[4–6] but usually it is a c inhabitant of the intestine Recently there has renewed interest in the idea that the pre *Cl welchii* in the intestine should not be without further inquiry into its possible asso with various intestinal disorders, including diarrhœa which sometimes complicates operations[7,8] BRUCE[9] attributes such disorde postoperative disturbances of blood supply ischæmia in parts of the intestinal mucosa— which does not necessarily conflict with the gestion that *Cl welchii* may participate in causation of these postoperative disorders o intestine, since reduced oxygenation resulting ischæmia would certainly favour growth o organism Those who, like BRUCE, doubt wh *Cl welchii* plays much or any part in these intestinal disorders can point to the mildness syndromes that have been ascribed to *Cl* type A COLLEE[6] reported that in one outbr food-poisoning caused by *Cl welchii*, of 300 at risk only 25 had symptoms DACK et al[10] cluded, from the difficulty of producing illn volunteers fed *Cl welchii*, that further evid required before this organism was regarded cause of the food-poisoning symptoms ascribed But none of this is likely to disturb those who that *Cl welchii* may have been underestimated intestinal pathogen in man *Cl welchii* type D, status as an intestinal pathogen of sheep is doubt, is found in the intestine of healthy s and cultures of the organism do not produce sym when fed to sheep, unless simultaneously morphine is administered to paralyse int movement[3] The mere presence of *Cl welchii* obviously not enough to cause an intestinal distur either in sheep or in man , and it is importan learn more about the conditions which favour prevent pathological effects One of the preven influences may be a substance or group of substan neutralising *Cl welchii* α toxin which D et al[8] found in the human intestine

Possibly the most serious of the pathological eff confidently attributed to *Cl welchii* in the hu intestine is the "enteritis necroticans" described b ZEISSLER and RASSFELD-STERNBERG[11] This se

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[1] Williams B W *Brit J Surg* 1926 14 295

[2] Williams B W *Lancet* 1927 i 907

[3] Bennetts H W *Bull Coun sci industr Res* 193 no 57

[4] Hobbs B C Smith, M E Oakley C L, Warrack G Cruickshank J C *J Hyg Camb* 1953 51 75

[5] Oakley C L , Warrack, G H *Ibid*, p 102

[6] Collee J G *J R Army med Cps* 1955 100 46

[7] Howie J W Duncan I B R Mackie L M *Lancet* 19 ii 1018

[8] Duncan I B R. Goudie J G Mackie L M Howie J *J Path Bact* 1954 67, 282

[9] Bruce J See *Lancet* 1954, ii 1204

[10] Dack G M Sugiyama H Owens F J Kirsner J *infect Dis* 1954 94 34

[11] Zeissler J Rassfeld Sternberg, L *Brit med J* 1949 See also Fick K A Wolken, A P *Lancet* 1949 i 51

ler is often marked by hæmorrhagic enteritis and hing of the mucosa, and the patient may die dehydration, circulatory failure, or intestinal uction The form of *Cl welchii* regarded as the of enteritis necroticans is unusually resistant at surviving 100°C for one to four hours, and is n as type F But those who hold that *Cl* *ii* type A may be a pathogen of the human me have derived much of their thinking not the findings in enteritis necroticans, but by from the unequivocal evidence of the effects *welchii* type D in sheep *This organism in turn* irst seriously considered as a pathogen because ILLIAMS's work on *Cl welchii* in the human ine Now the circle is completed by the reports we publish this week that *Cl welchii* type D has isolated from lesions of the human intestine LEESON WHITE and Dr BULLEN (p 384) found rganism and its ε toxin in the intestinal contents fatal case of acute obstruction of the small intes Dr KOHN and Dr WARRACK (p 385) isolated ice from a patient who had mild postdysenteric with violent attacks of diarrhœa, this patient detectable amounts of ε antitoxin in his blood e two reports will help to keep the debate going, will contribute to the interest of investigating ôle of *Cl welchii* in intestinal disorders by adding her type of this organism to be sought—happily pe whose toxin can be clearly demonstrated in ral material from the intestine

## Enuresis

HE causes of bedwetting are still in dispute is hardly surprising since the physiology of urition in man is still not fully understood over most of the patients are children with m communication is less easy than with adults the interpretation of the results of treatment is willed by the tendency of enuresis to spontaneous However much argument there may be about relative importance of emotional factors, social ronment depth of sleep constipation, and so h, no-one questions the necessity to exclude nic disease of the urinary tract Gross organic ase accounts for only a small proportion of cases r example 10% of NASH's[1] series of 218 Over of these patients with organic disease had reten with overflow—a gross disorder indeed—and e of the others had conditions detectable only special investigations such as urethral polypi ic kidney and bladder tumour Probably still re refined investigation would show that organic ase accounts for enuresis more commonly than now supposed FISHER and FORSYTHE,[2] of lfast have described their experience with a w technique of cysto urethrography in 135 children er five years of age whose enuresis had not ponded to three months intensive medical or ychiatric treatment or both Voiding cysto ethrography is a well recognised method of investi ting abnormalities of micturition and the chief velty of the technique devised by FISHER and ORSYTHE is the use of a 25% suspension of barium lphate which throws an extremely dense shadow d so traces the outline of the urethra in the finest detail Their results are remarkable Of the 135 children no less than 25 showed evidence of valves of the posterior urethra This proportion may be compared with NASH's 1 valve in 218 enuretics In only 5 of the Belfast cases was there clinical evidence of obstruction (dribbling or straining), and no information is given about residual urine (except that it was measured routinely) or trabeculation We know that severe obstruction may be caused by valves in the posterior urethra, and in such cases the patient may have overflow incontinence and present as an enuretic We are on less sure ground in inferring that a fold of mucous membrane in the posterior urethra if it does not cause obstruction may yet cause enuresis There are indeed normal folds running outwards from the lower end of the verumontanum and the question arises as to the extent to which such folds if well developed but still within normal limits, may be shown up in the fine detail of these new urethrograms The technique of FISHER and FORSYTHE deserves a wide trial, but the results must be interpreted cautiously

Many children with enuresis have normal frequency by day, which shows that their bladders have a normal capacity Why then should their bladders hold less at night? Do they in fact hold less? Perhaps they are called on to hold more by failure of the kidneys to shut down for the night in the normal way, and certainly many distracted mothers express themselves forcibly about the quantity of urine in the bed POULTON[3] found that in most enuretics there is a disturbance of the normal rhythm which he calls relative nocturnal polyuria It has been stated that normally about four and a half times as much water is excreted by day as by night POULTON[3] found that in normal children the lowest day night ratio was 1 8 whereas of 100 enuretics 69 had a day night ratio of less than 1 8 The significance of this finding is by no means obvious It certainly cannot wholly explain enuresis, for polyuria due, for instance to diabetes insipidus is not particularly associated with enuresis It may be one of several primary factors, or perhaps it is a secondary effect of enuresis It may be due to the emotional disturbance caused by (or possibly *causing*) bedwetting emotion is a well known cause of diuresis A second possibility is that a primary abnormality of the bladder neck causes enuresis and also incidentally polyuria WINSBURY WHITE[4] has noted polyuria in association with posterior urethritis and the characteristic nocturnal frequency of prostatic patients is due to nocturnal polyuria We have much to learn about abnormalities of excretory rhythm in diseases of the lower urinary tract

Is enuresis caused by an abnormality of sleep? No less an authority than MEREDITH CAMPBELL[5] bluntly says No Nevertheless many are convinced that the lightening of sleep by such drugs as dexamphetamine often stops enuresis This does not prove that deep sleep is a cause For one thing dexamphetamine does not only lighten sleep it has a local action on the neuromuscular mechanism of the bladder[6] similar to that of ephedrine which has been used for some time in the treatment of enuresis

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Nash D F E Ann R Coll Surg Engl 1949, 5 318
isher O D, Forsythe W I Arch Dis Childh 1954 29 460
[3] Poulton E M *Lancet* 1952 ii 906
[4] Winsbury White H P Textbook of Genito-urinary Surgery Edinburgh 1948 p 260
[5] Campbell, M Urology London 1954 p 1636
[6] Cartwright H *Brit med J* 1951 i 1030

Conversely NASH [7] suggests that ephedrine may be effective because of its stimulating and sleep diminishing effect, and not its local action on the bladder Belladonna and ephedrine have a modern counterpart in methanthelinium bromide ('Banthine') This very effective ganglion-blocking agent has been shown to abolish the uninhibited contractions that occur in the bladders of some enuretics But like many effective remedies, methanthelinium will fall into disrepute if used indiscriminately, in enuresis it should be reserved for cases with uninhibited contractions

Whatever the primary cause or causes of enuresis, the immediate fault is the failure to wake when the bladder empties, and a direct attack may be made at this point Parents often waken the child shortly before they think the wetting is due to take place, or an alarm-clock may be used for this purpose These methods are disappointing But if the full bladder fails to ring a bell figuratively, the emptying bladder may be made to ring a bell actually and so establish a simple conditioned reflex This method is perfectly sound, provided that al factors are also treated and organic disease is ex The patient lies on a pad containing an open circuit which is closed immediately the pad is by an electrolytic solution (urine), and this bell This method, introduced some years the U S A,[8] has been tested in this DAVIDSON and DOUGLASS [9], and last year Bo reported from Australia that it had proved in 8 out of 12 patients The method has advantages The apparatus is expensive, and delicate, and it can be used by only one at a time, the method requires the cooperation of the child, and establishing the tioned reflex may take many weeks Nevert method, based on such sound physiological has much to commend it We are not so well e to treat enuresis that we can ignore any technique

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[7] Nash D F E *Lancet* 1950, ii, 486

[8] Mowrer O H *Amer J Psychiat* 1938 51, 163 Mowr, Mowrer, W M *Amer J Orthopsychiat* 1938 8 436

[9] Davidson, J R, Douglass, E *Brit med J* 1950, i, 1345

[10] Bostock, J *Med J Aust* 1954, ii 141

# Annotations

## THE PITUITARY AND PIGMENTATION

THE pituitary glands of vertebrates secrete a hormone variously called melanocyte stimulating hormone (M S H), melanophore expanding hormone, and intermedin, whose target organs are the pigment cells—principally those of the skin In amphibia these pigment cells can quickly darken the skin by expanding black tendrils under the direct influence of M S H In mammals the pigment cells are stimulated by M S H to synthesise more melanin, which darkens the skin more slowly than the mechanism in amphibia Since the original report by Jores [1] in 1933 several workers have demonstrated this activity in human blood, and in this week's issue Dr Hudson and Dr Bentley show that man, like other animals, has melanocyte stimulating hormone (they prefer to call it melanophore expanding hormone) in his pituitary

Lerner and his group at Portland, Oregon,[2] injected into volunteers large amounts of a preparation of M S H containing very little corticotrophin or other pituitary hormone They describe specific, if somewhat cumbersome, methods for urinary and blood assay of the hormone [3] This is important, since biological assay depends on changes in colour in isolated frog's skin, and various substances, contained in blood and urine, which are not pituitary hormones affect the result Lerner has defined the normal limits for M S H in blood and urine, and has shown these to be the same for men and women and for albino, white, and coloured people During pregnancy excretion of M S H increases progressively from the eighth or ninth week until term, after which it reverts to normal in a few days Excretion of M S H was increased in some patients with Addison's disease, and in others after bilateral adrenalectomy Cortisone inhibited heavy excretion of M S H Administration of M S H led to darkening of the skin and formation of new pigmented moles—evidence that the hormone causes multiplication of melanocytes as well as increased melanin synthesis Some deepening of skin colour was detectable as early as ten hours after high doses

It is now clear that skin darkening produced by commercial preparations of corticotrophin is due to contamination by M S H For some time it was difficult to separate these hormones, and it seemed possible that corticotrophin and M S H were one and the same M S H, unlike corticotrophin, is stable to alkali[5] ( plete separation of the activities is *difficult*, purest M S H. may possibly have a slight corticotrophin like effect [6] Are these two in fact in Nature? In man, at any rate, they may not Many states associated with general increa pigmentation are known to be associated also increased production of corticotrophin, and cortical hormones inhibit both corticotrophin and

There is still no good evidence that M.S.H causes pigmentary disturbances as melanomatosis, re pigmentosa, or vitiligo In man this hormone see be a kind of endocrine vestige, of little importan metabolism and survival but of great interest to icians because it is the inseparable twin of corticotr and hence in certain conditions skin pigmentation guide to corticotrophin production Much remain learnt Is there in man a melanocyte inhibiting hor analogous to that described for fish by Enami,[8] foreshadowed by the earlier work of Hogben?[9] the placenta produce M S H, as might be expected indeed produces corticotrophin?[10] At just what in melanin synthesis does M S H act? With their met of assay Dr Lerner and his colleagues may be ab answer these and other questions

## CANCER CLUES

Edgar Allan Poe once wrote of an object b successfully hidden almost literally under the sear nose Perhaps some vital clues in the cancer my may similarly lie under our noses, awaiting disco by an astute observer There have lately been reminders of such a possibility—one from Israel and other from Arizona

Dr Kalman J Mann, director of the *Hadassah Med* Organisation in Israel, has stated[11] that not a single of lung cancer has been reported among Yemenite in Israel in the last fifteen years Dr Mann pointed that these people do not smoke cigarettes but do smok a narghile—an oriental pipe in which tobacco smoke drawn through water An extensive investigation

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[1] Jores, A. *Z ges. exp Med* 1933, 87, 266

[2] Lerner, A. B Shizume K., Bunding, I *J clin Endocrin* 1954, 14 1463

[3] K., Lerner, A B *Ibid*, p 1471

[4] *Lancet*, 1952, i, 1150

[5] Morris, C J O R *Ibid* p 1210

[6] Benfey, B G Saffran, M Schally A V *Nature, Lond.* 19 174, 1106

[7] Sulman, F G *Lancet*, 1952 ii, 247

[8] Enami M. *Science*, 1955, 121, 36

[9] Hogben L, Slome D *Proc roy Soc* B 1931, 108, 10, 1936, 120, 158

[10] Opsahl, J C, Long, C N H *Yale J Biol Med* 1951, 24

[11] *New York Times*, Feb 1, 1955

a started with the purpose of establishing the cause
his remarkable finding From Arizona the public-
th commissioner Dr Clarence G Salsbury, has
rted[11] somewhat similar findings, with reference to
er generally among the Navaho Indians Apparently
eer is hardly ever found in the 75 000 Navahos In
dy of the records of all hospitals serving these
ple, Salsbury and his associates discovered in 1953
60,000 admissions had included only 208 cases of
er and the 118 cases in females included no more
3 instances of cancer of the breast Salsbury
eves that the Navaho diet may be the key to the
parative lack of cancer Highly refined foods are
nt from the typical diet which consists mainly of
, corn squash, some fruits and nuts herbs native
and 'squaw bread —a type of crisp panbread "

## PIONEERS IN PSYCHIATRY

HREE years after the fall of the Bastille, Philippe
l struck the chains from the lunatics in the Paris
tre To the student of medical history—as the
ussion at a meeting on Jan 8 of the section of
chiatry of the Royal Society of Medicine showed—
action is significant not only as a landmark in the
elopment of psychotherapy but also as a reflection
he spirit of his age Indeed all his achievements
r witness to the influence of that ' Age of Enlighten
nt ' As Prof Aubrey Lewis pointed out Pinel
ly the importance of applying the mathematical
the exact sciences then making their appear
icine He was among the first to evaluate
treatment statistically and to appreciate
e case records regular progress notes,
therapeutic trials. In the field
l was much indebted to British writers
ke—and by his humane treatment of
set an example which was followed

most enthusiastic disciples was the
les Prichard, who combined an
ethnology and philology with an
ty well in advance of his times
work the *Treatise on Insanity*
nch influence and in particular
Esquirol Dr A D Leigh,
ons to British psychiatry
first to distinguish moral
s of mental disorders—a con
since received little favour
o of his Quaker upbringing
secure more humane con
ardent support of the anti
he became physician to the
learning skill and energy
physician with enlightened

had advocated a humane
sane William Browne,
yal Hospital Dumfries
led it with outstanding
ussing Browne s thesis,
*hat They Ought To Be*
ception of a mental
lern times Browne
uld be well planned
palace of a peer —
in which patients
and the freedom
ppreciated to the
py his patients
each day with a
games
and even the
production of plays He was, moreover an excellent clinician keeping copious notes on the progress and treatment of each of his patients, making systematic records of their dreams and including in each case history a philosophical analysis of the patient s mind.' Browne held that the staff of mental hospitals should be the companions, friends, and teachers of their patients as well as their guardians and he continually recommended " moral treatment of the most extended and exquisite form ' In his hands the methods championed by Pinel and Prichard at last found full and practical expression

## CHLORPROMAZINE FOR HICCUP

It is not surprising that chlorpromazine should be tried in the treatment of hiccup for the drug powerfully inhibits many central reflexes[1] and hiccup may sometimes represent the motor component of a reflex pathway —although there is good evidence that this is not always so[2] Certainly the results now claimed by Friedgood and Ripstein[3] are impressive 50 patients with hiccup attributed to various causes ranging from coronary thrombosis to thoracic abdominal and urological operations were treated with chlorpromazine and in 41 a single intravenous dose of 50 mg stopped the hiccups. Some of these responses can best be described by the favoured epithet, dramatic for example in a man aged 57 who had had hiccups for nine days after an operation for cancer of the rectum the hiccups stopped three minutes after the injection of chlorpromazine and did not return Chlorpromazine will presumably now take its place in the list of remedies to be tried in the treatment of intractable hiccup

## WATER ABSORPTION

When heavy water is placed in the stomach or small bowel serial samples of arterial blood show the presence of deuterium within a few minutes The level of deuterium in the arterial blood reaches a peak at about ten minutes after intestinal administration but at thirty minutes after gastric administration The disappearance of intravenously injected deuterium can be estimated, and used to correct the curves obtained after alimentary administration so giving a measure of the rate of absorption By such studies Scholer and Code[4] estimate that moderate quantities of water placed in the stomach are absorbed at a rate of 2 5% of the dose per minute; absorption from the small bowel is much more rapid—26 1% per minute They point out that water in the stomach remains in a puddle' demonstrable by suspended barium whereas water introduced into the intestine is rapidly dispersed over a large mucosal surface Even allowing for this, the absorptive activity of the small intestine which has been shown to be an active process[5] is probably greater than that of the stomach the demonstration that appreciable water absorption goes on in the stomach confirms in man the findings in isolated gastric pouches in the dog[6]

The deuterium method of studying water absorption has been applied to the practical problem of whether to give water by mouth to patients with abdominal and other injuries This work reported by Howard,[7] may have set up a record in long range collaboration for the deuterium was given in Korea and was estimated in Washington D C The assessment of absorption in this study was based not on the form of the early arterial curves but on the time taken to reach equilibrium judged by constancy of the deuterium level in venous plasma In healthy controls equilibration was complete in two hours In patients with chest and limb injuries equilibrium was somewhat delayed, but this may have been due to delay in distribution of absorbed deuterium, for deuterium given intravenously left the circulation more slowly in injured patients In the patients with chest and limb injuries fluid given by mouth was effective in controlling thirst and maintaining the output of urine By contrast, in patients with abdominal wounds equilibration after oral administration of heavy water was grossly delayed, the delay in absorption was greatest when the patient was shocked, but persisted in some degree for a few days after shock had been corrected More direct evidence of interference with water absorption was found at operation, when the bowel was often distended with unabsorbed fluid, and patients with abdominal injuries commonly vomited if given water in any quantity

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[1] See *Lancet* Feb 12 1955 p 337
[2] *Ibid* 1954 i, 601
[3] Friedgood C E Ripstein C B *J Amer med Ass* 1955 157 309
[4] Scholer J F, Code C F *Gastroenterology* 1954, 27 565
[5] Visscher M B Fetcher, E S, Carr, C W Gregor H P, Bushey M S, Barker, D E *Amer J Physiol* 1944 142 550
[6] Cope, O Blatt, M H, Ball, M R *J clin Invest* 1943 22 111
[7] Howard J M *Surg Gynec Obstet* 1955 100 69

This type of study cannot tell us whether delayed absorption of water is due to diminished peristalsis, to diminished blood-flow, or to a specific impairment of water absorption by the intestinal mucosa, but it justifies the practical recommendation that fluid should not be given by mouth to patients with major abdominal injuries With extra abdominal injuries there may be some delay in water absorption, but this is of no practical importance, and the patients can be given enough water by mouth to relieve thirst and maintain urine volume This advice should perhaps be qualified by the reminder that oliguria is to be expected for twenty-four to forty eight hours after a severe injury, and water intake should not be excessive during this period, in view of the risk of water intoxication [8]

## HEALTH AND GROWTH OF THE UNDER-FIVES

COMPREHENSIVE long term field studies in human biology and sociology are now yielding rich harvests Nowhere is this approach providing more valuable information than in the field of child health, where three such surveys have attracted wide attention The first was the Luton survey [9] of 1498 children born there in 1945, of these, 1322 were followed up for the first five years of life The second survey began in 1946 when a joint committee of the Institute of Child Health (University of London), the Society of Medical Officers of Health, and the Population Investigation Committee inaugurated a nation wide survey based on 5386 of the children born in the first week of March of that year, this study continues and the children are to be followed up to the age of 12 years A third field study, conceived by the late Sir James Spence, began in Newcastle upon Tyne [10] in 1947 with the enrolment of the 1142 children born in that city in May and June, this study, which also continues, is especially important since it embraces the family of each child

The nation-wide survey has already led to the publication of fifteen reports on various aspects of maternal and child health The latest report [11] summarises some of the findings relating to the first five years of life Low social class, high parity of the mother, and premature birth are all shown to impose a handicap on health It was also found that in passing from the lowest to the highest social group the number of families with four or more children fell rapidly Although later-born children tended to be heavier at birth than the early ones by the age of 2 years they had fallen behind in weight and they remained behind at 4 years, they we also smaller than first born children at these ag A comparatively high proportion of the underweig children were the later born children of large famili The lower social groups thus provided more than the fair share of stunted and underweight children a proportionately fewer physically superior children Th reasons are not discussed in the preliminary summar but genetic factors and, particularly, nutritional facto will probably both prove important

Children in large families and lower social groups r a much greater risk of contracting infectious disea early in life—when the consequences are likely to b more serious Overcrowding was an important co tributory factor, for among the families of man workers lower respiratory infections in the first 2 ye of life were one and a half times more frequent in hom with two or more persons to a room than in those wi one to a room or one to more than one room Ove crowding is still much more prevalent in Scotland th in England, and this probably explains the considerab greater hospital admission rate for respiratory infectio in Scotland By the age of 5 years one child in fi had been admitted to hospital at least once, and late born children were admitted more often than first bo Rather unexpectedly accidents were as frequent well-to do as in poor homes and in small families as large ones

About 25% of the mothers did some paid work, the effect of the opposing influences of increased fam income and deprivation of continuous maternal ca were studied There is no evidence so far that the hea of the children suffered when mothers went out to wo except for a greater incidence of infection at an ea age caused by a higher proportion of such children be cared for in day nurseries The psychological trau induced in these circumstances by separation from mother is not discussed in the preliminary report, is no doubt receiving attention

The survey has confirmed the general impression th the mothers who use child welfare clinics are the mo careful and conscientious and those who least ne advice, and that it is the mothers of large families w make least use of such centres In all social cla first born children were the most likely to be tak while those in families of three or more children w the least likely to be taken, such children were n given regular medical supervision until they went school It is easy to appreciate the difficulty of ta the younger children to a clinic when there are sev in the family, and it is understandable that the mot of several children may feel that she no longer nee advice But the much lower rate of diphtheria immun sation in the younger children of large families is a go example of the less satisfactory care given to su children whereas 80% of the first born had be immunised by the age of 2 years, only 50% of the young children of large families were so protected 11% the mothers were considered to be giving their childre only fair or poor care, they came from the poorest an most overcrowded families with many children and rare went to child-welfare clinics

The full significance of the facts that are bein collected in the survey will not be apparent until it i possible to look back and see events in the life of th child as components of a continuous chain

THE INDEX and title page to Vol II, 1954, which wa completed with THE LANCET of Dec 25 is now i preparation A copy will be sent gratis to subscriber on receipt of a postcard addressed to the Manager o THE LANCET, 7, Adam Street, Adelphi, W C.2 Subscribers who have not already indicated their desi to receive indexes regularly as published should do s now

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[11] The Health and Growth of the Under Fives By a Joint Committee of the Institute of Child Health (University of London) Society of Medical Officers of Health and Population Investigation Committee National Survey of the Health and Development of Children London School of Economics and Political Science 13 Endsleigh Street London, W C 1 Pp 17

# Social and Biological Factors in Infant Mortality *

## II VARIATION OF MORTALITY WITH MOTHER'S AGE AND PARITY

J A HEADY
MA Oxfd

C DALY
B Sc Glasg

J N MORRIS
MA Glasg., M R C P., D P.H

OF THE SOCIAL MEDICINE RESEARCH UNIT

...e inquiry deals with social and biological influences ...the stillbirth and infant mortality rates for the 1½ ...on children born in England and Wales in 1949 and ... Information obtained when ... deaths were registered is ...d to information obtained ...n the children were born The ... paper in the series stated ... objects and methods of the ...ry as a whole The present ...st describes the main features ...e variation of the stillbirth ..., and the neonatal and post...atal mortality rates with ... "biological" factors—the ...of the mother at the birth of ...child, and her parity Births ...49 only are considered

...e pattern of variation has ...ously been established on ...ound statistical basis for ...irth rates and neonatal ...ality-rates though for the ...ntal period (the first four ...s of life) the only series ...h is large enough to permit a ...actory discussion of the ...tion with both mother's ...and parity at the same time ... with births in New York ... in 1936–38[12] For post...atal deaths—that is deaths ...e first year of life after the ...four weeks—there are no ...ed data based on large ... numbers to permit de...analysis. Three studies of ...post-neonatal death rate from ... point of view[5 6 7] do how...r agree on essentials The ...ther's age and her parity are ...ortant in the mortality of ... after the first month the ... rates fall fairly regularly ...e mother's age for mothers ...a given number of children ...crease with size of family ...mothers of a given age There is thus a marked ...ast with stillbirths where the youth of the mother ...advantage at any parity and in considering mothers ... age a first birth is at higher risk compared ... other births

### Results from this Inquiry

...s for the 691 949 single legitimate live and ...births that occurred in England and Wales in 1949 are given in simplified form in figs 1 and 2, and in greater detail in the table the three parts of which correspond with the three parts of each figure There were 14,870 stillbirths, 11,069 neonatal deaths and 7545 post-neonatal deaths amongst these births representing a loss of 5% between the 28th week of pregnancy and the end of the first year of life (Multiple and illegitimate births are not considered in this paper They form only 7% of all births )†

The figures show the same data arranged in two different ways In fig 1 the emphasis is on how the mortality rates vary with the age of the mother when women of a given parity ‡ (or parities) are considered

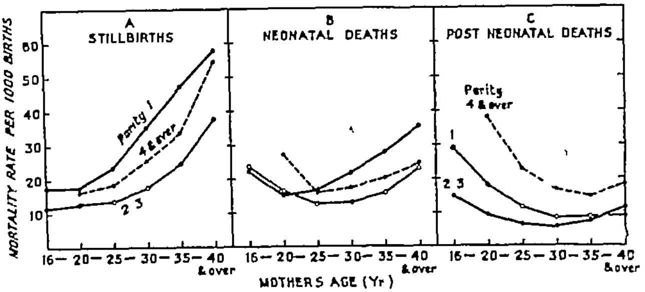

Fig 1—Variation with mother's age of stillbirth and infant-mortality rates (mothers of different parities compared)

Single legitimate births in England and Wales, 1949 Stillbirth rates per 1000 live and still births other rates per 1000 live births.

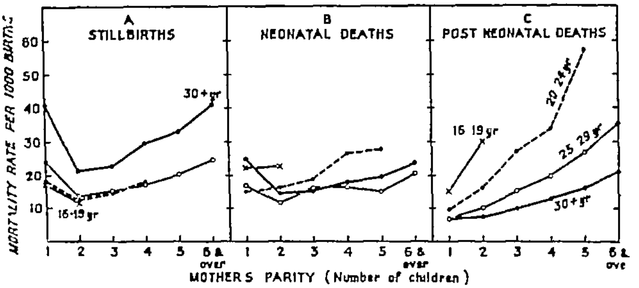

Fig 2—Variation with mother's parity of stillbirth and infant-mortality rates (mothers of different ages compared)

Single legitimate births in England and Wales, 1949 Stillbirth rates per 1000 live and still births; other rates, per 1000 live births

fig 2 places the emphasis on the variation with parity for mothers in a given age group The figures correspond therefore with reading the three parts of the table (1) across for mothers of a given parity and (2) down for mothers of a given age To make the diagrams clearer however certain mothers age groups and parities have been amalgamated It is considered that the particular

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* ... articles reporting an inquiry made jointly by the ...Medicine Research Unit (Medical Research Council) ... the General Register Office The articles[1] were ...ned by the Unit in collaboration with the General ...er Office and have been approved for publication ...the joint working party responsible for the inquiry

† 1949 was an ordinary year for infant mortality The striking improvement of the rate in 1948 (33 9) compared with 1947 (41 4) was maintained in 1949 (32 4) There was no particular excess of mortality from any infectious disease in 1949

‡ The parity of the mother is defined here as the number of children she has borne—surviving dead or stillborn—including the present one

amalgamations chosen have not obscured anything important

### *The Range of Variation*

There is *a wide range of variation in the stillbirth-rate* and the post-neonatal mortality-rate with both age and parity The range shown in the table for stillbirths (A) is from 11 6 per 1000 to 90 0, and in the table for post-neonatal deaths (C) from 5 5 per 1000 to 56 9 The smoothness of the general trends (with minor exceptions) shows that the high figures are not freaks but represent real risks Those mothers and children who are exposed to the very high rates on account of unfavourable age *and parity—though numbered in tens of thousands* even in one year—are nevertheless a small minority The range of variation of the neonatal mortality-rate with age and parity is much less than that of either the stillbirth or the post-neonatal rate

### *Differences in Pattern*

Figs 1 and 2 show clearly that the *pattern* of variation is different for the three mortality-rates Considering first the variation with mother's age for any particular parity, or group of parities (fig 1), the pattern for post-neonatal deaths can be seen to be almost the rever that for stillbirths For stillbirths increased age ı adverse factor at any parity, witness the low rat mothers under 20 in fig 1 and the high rates for mo over 30 in fig 2 , while for post neonatal deaths incre age appears to be a favourable one until 35 years (fi though the rates become higher after that In the four weeks of life extremes of both age and youth i mother seem to be unfavourable

The variation with the number of children, mothers of a given age are considered (fig 2) is also different for stillbirths and post-neonatal deaths I stillbirths there is the familiar high risk for first b followed by a sharp fall, and a gradual rise for children which is particularly noticeable in the mothers For post neonatal deaths, on the other there is a steady rise with increasing parity in age group, witness the low rates for first childre fig 2, and the high rates for fourth and later childr fig 1 The rise is sharper for the younger moth those under 25 years of age—than for the older mot Once again the neonatal mortality-rate seems to oc an intermediate or transitional position

TABLE OF STILLBIRTH AND INFANT MORTALITY RATES VARIATION WITH MOTHER S AGE AND PARITY SINGLE, LEGITIMATE BIRTHS, ENGLAND AND WALES, 1949

| Mother s parity (no of children) | Mother s age (years) | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | 16–19 | 20–24 | 25–29 | 30–34 | 35–39 | 40–44 | 45 and over | All ages |
| A. STILLBIRTHS * | | | | | | | | |
| 1 | 17 2 | 17 7 | 23 5 | 35 3 | 47 2 | 58 2 | | 23 3 |
| 2 | 11 6 | 12 3 | 13 3 | 17 4 | 23 7 | 39 5 | | 15 5 |
| 3 | | 14 6 | 14 9 | 18 0 | 26 0 | 34 6 | 58 0 | 18 7 |
| 4 | | 17 3 | 17 1 | 25 4 | 28 3 | 49 1 | 75 6 | 25 3 |
| 5 | | | 20 2 | 23 9 | 34 0 | 49 1 | 87 2 | 29 8 |
| 6 | | | 25 0 | 28 1 | 39 6 | 65 3 | 69 2 | 37 2 |
| 7 | | | 18 8 | 25 5 | 34 5 | 51 9 | 81 5 | 35 3 |
| 8 | | | | 29 0 | 33 8 | 51 4 | 70 4 | 39 0 |
| 9 | | | | 35 3 | 37 6 | 53 4 | | 44 3 |
| 10 or more | | | | 49 2 | 46 1 | 57 4 | 90 0 | 54 7 |
| All parities | 16 7 | 16 1 | 17 9 | 23 4 | 31 5 | 47 6 | 68 0 | 21 5 |
| B NEONATAL DEATHS (at ages under 4 weeks) † | | | | | | | | |
| 1 | 22 2 | 15 2 | 16 5 | 21 4 | 27 8 | 33 8 | | 17 7 |
| 2 | 22 4 | 15 9 | 11 6 | 12 4 | 15 6 | 23 1 | | 13 6 |
| 3 | | 18 5 | 15 9 | 14 1 | 16 4 | 21 5 | | 16 1 |
| 4 | | 20 2 | 16 2 | 15 6 | 18 5 | 21 4 | | 17 6 |
| 5 | | 27 2 | 14 7 | 17 8 | 21 0 | 15 6 | | 18 1 |
| 6 | | | 15 8 | 21 0 | 21 0 | 21 4 | | 20 5 |
| 7 | | | 26 9 | 16 3 | 18 6 | 25 6 | | 21 1 |
| 8 | | | | 21 1 | 25 9 | 31 7 | | 26 6 |
| 9 | | | | | 13 3 | 37 2 | | 24 2 |
| 10 or more | | | | | 25 4 | 28 0 | 42 4 | 28 5 |
| All parities | 22 4 | 15 7 | 14 5 | 15 7 | 19 2 | 24 2 | 37 0 | 16 4 |
| C POST NEONATAL DEATHS (at ages 4 weeks–1 year) † | | | | | | | | |
| 1 | 14 8 | 9 1 | 6 3 | 5 5 | 7 2 | 11 3 | | 8 3 |
| 2 | 29 1 | 15 9 | 9 8 | 6 9 | 7 6 | 7 2 | | 10 7 |
| 3 | | 26 4 | 14 8 | 9 9 | 9 4 | 9 6 | | 13 7 |
| 4 | | 33 5 | 19 2 | 13 1 | 11 6 | 12 7 | | 15 7 |
| 5 | | 56 9 | 26 5 | 18 1 | 13 7 | 15 2 | | 19 1 |
| 6 | | | 31 5 | 16 5 | 16 6 | 17 4 | | 19 0 |
| 7 | | | 48 0 | 26 7 | 20 1 | 16 4 | | 23 5 |
| 8 | | | | 27 0 | 19 2 | 17 7 | | 20 4 |
| 9 | | | | 26 8 | 17 7 | 29 5 | | 24 2 |
| 10 or more | | | | | 24 0 | 27 4 | | 26 1 |
| All parities | 16 4 | 12 6 | 10 4 | 9 2 | 10 4 | 13 6 | 19 4 | 11 1 |

* Per 1000 live and still births † Per 1000 live births

Mother s age refers to age attained on her last birthday before the present birth

Mother s parity refers to the number of children surviving dead or stillborn (and including the present birth) by the mother's present and any previous husband Abortions before 28 weeks of pregnancy are excluded

The absence of an entry indicates that there were fewer than 10 stillbirths neonatal deaths or post neonatal deaths in the cell

The table is based on 676 770 live births and 14,870 stillbirths Of these there were a total of 3830 or 0 6 % for which the mother's age or parity (or both) was not stated No attempt is made to distribute these births proportionately in the table but they are included in the total rate and, where appropriate in the " All ages ' and All parities ' figures (Details of the distribution of births and stillbirths will be found in the Registrar General s Statistical Review of England and Wales, 1949 Tables part II Civil p 128 )

## Comment

For the first time data have been presented national scale which show the relationship of mat age and parity, consecutively, to fœtal deaths aft weeks of pregnancy, to deaths in the first four wee life, and deaths in the remainder of the first year *results are in broad agreement with previously publ* work, and in particular they confirm and amplif earlier indications of post neonatal trends, though were based on much smaller numbers The cont between the three rates add interest to the results are an example of the value of the cohort appro following a particular set, or " cohort," of births

In keeping with the general objects of the inquir next steps will be to examine how the effects o mother's age and parity are modified in different circumstances [2 9], how much the different caus death, in so far as they are known, contribute t variation with age and parity [4], and to trac emergence of the striking post neonatal patter breaking down the ages at death into the first day o the first week, the next three weeks, and so on parison of the patterns for stillbirths with thos deaths at various times in the first month of life have considerable bearing on the choice of the best of deaths to regard as " perinatal "—stillbirths deaths in the first day, for instance, or the first wee the first four weeks

Most of this finer analysis will be more depen when the 1950 data can be added Meanwhile, a statements can be made on the single year's figures have so far been examined

*First* it can already be stated, in terms of *factors, that the characteristic pattern of variation* age and parity for each of the three mortality rat present *within* each social class

*Second* since large families are associated w relatively high post neonatal death-rate, and since, last half century, families have decreased in size an post neonatal death-rate has fallen spectacularly ( 91 per 1000 in 1906 to less than 10 today) it is natu ask whether the reduction in family size accounts f important part of the fall in the rate Although no statement can be made in the absence of the nece detailed information on the rate for mothers of diff ages and parities in 1906, the table contains the part of the answer to this question In part C, very rates are above 30 , and it can be shown that les 6% of births are subject to a rate greater than 2 1000 It follows that even for the large families, so hich still exist the rate is now very much lower than , and that whatever the circumstances prevailing in 06, the change in family size by itself cannot conceivably re made more than a small contribution to the over all line in the rate.[7]

Third the strong relationship which emerges between ternal age and parity and the post neonatal mortality e is of interest It is well known that age and parity re related to the stillbirth rate and not surprising— e these factors are obviously relevant and it is ible to envisage connections with the maternal natal, and fœtal pathology involved A relation tween age and parity and later mortality does not so closely from these considerations and it is more interesting therefore, that these factors do d post-neonatal mortality, and that the effect is so nt.[10]

tillbirths and post-neonatal deaths thus appear as groups with different secular trends (for instance 1948), different typical causes and now, quite nt variations with age and parity Post neonatal ths are due mainly to infections and as might be cted the deaths from infection are related to mother's and parity in much the same way as the total of hs at this age.[1 6 7 8] They are also as is well known ly sensitive to differences in social circumstances trends of post neonatal mortality with age, parity social class may therefore furnish clues to the spread control of the infections At least three lines of nation present themselves: (1) the increased oppor ity for infection in a large family (opportunity avated, it may be, by overcrowding) (2) other mic consequences of the large family at most levels come; and (3) the ability or inability to "cope" of mothers with large families, particularly those in e circumstances.[11] All these are illustrations of combined action of social and biological factors

n terms of a main objective of the present inquiry, at three "vulnerable" groups appear from the figures is paper

Mothers over 35, bearing first babies have a high risk of stillbirth.

Mothers over 40 of any parity have a high risk of stillbirth

Babies of young mothers with large families for their age have a high risk of death in the post neonatal period This applies to the youngest mothers having a second or later child, and to mothers aged 20–24 having a third or later child, for example

### Summary

The main features of the variation with the mother's and parity of the stillbirth rate the neonatal tality rate (deaths in the first four weeks of life) and neonatal mortality rate (deaths in the remainder the first year of life) are shown for England and Wales 49) There were 14 870 stillbirths 11 069 neonatal ths, and 7645 post-neonatal deaths amongst the 49 single legitimate births in that year The birth rate displays considerable variation, and so the post neonatal mortality rate but in a different The stillbirth rate rises with age for mothers of any parity whereas the post neonatal rate decreases e (except for mothers over 35) The stillbirth rate births of a given age is high for first births falls for nd and third births and rises thereafter; the post tal rate for children of mothers of a given age on other hand rises steadily with increasing parity natal mortality rate varies less than the other and appears to occupy an intermediate position implications are discussed

I am grateful to the staff of the General Register Office clerical, technical, and computing help; to colleagues criticism and advice; and to the staff of the Social Research Unit for clerical and computing work

*References at foot of next column*

# Reconstruction

## BUILDING HOSPITALS

### GREATER FLEXIBILITY AT LESS COST

ERIC MAIDMENT
Dipl Arch A.R.I.B.A., Dipl T P

IN the years before 1939 the increasing size of the hospitals that were being built all over the world reflected the growth of medicine and the change in its techniques This expansion suggested that it would soon be impossible to manage with the type of large permanent rigid hospital buildings which had evolved by slow traditional methods of design Most of them took five or six years to plan and build and yet it now seems that little attention was paid to the most efficient design of a hospital beyond a limited consideration of function and ventilation

The increasing complexity of modern methods of diagnosis and treatment means that more and more room is needed both in the wards and in the special departments of a hospital Developments in the various departments may often call for changes in size, in internal planning and in the relation of one department to another Moreover it is unlikely that the shortage of money which today hampers progress will be overcome in the next few decades so if we are to improve our hospital building in the near future we must do more than bring our designs up to date and make them more flexible we must make hospitals cheaper to build For these reasons most current ideas on medical planning and construction seem to me out of date, for they cannot provide the type of buildings now needed—and needed urgently in many parts of the world

If we are to overcome these difficulties the new buildings will have to set a new standard in quick and economical construction They should be capable of reasonable expansion or contraction and yet be economical to staff administer and maintain Moreover, despite all this the high quality of design and finish essential to a hospital must be maintained In underdeveloped parts of the world this fresh approach is vital, particularly where hospitals and clinics are to be built in places which have never had them before, where capital is desperately small and where doctors and administrators have to draw up their plans without knowing very clearly how the other medical arrangements will work out

One answer that is being evolved takes advantage in part but only in part of the experience that architects and builders have gained in building schools since the late war Here good use has been made of prefabrication —a device which has been known to succeeding civilisations under various names, though its successful industrial application has not yet been fully achieved Although the cost per place in these schools has been reduced despite a steady rise in general building costs prefabrication can never provide the main answer; for there has been little

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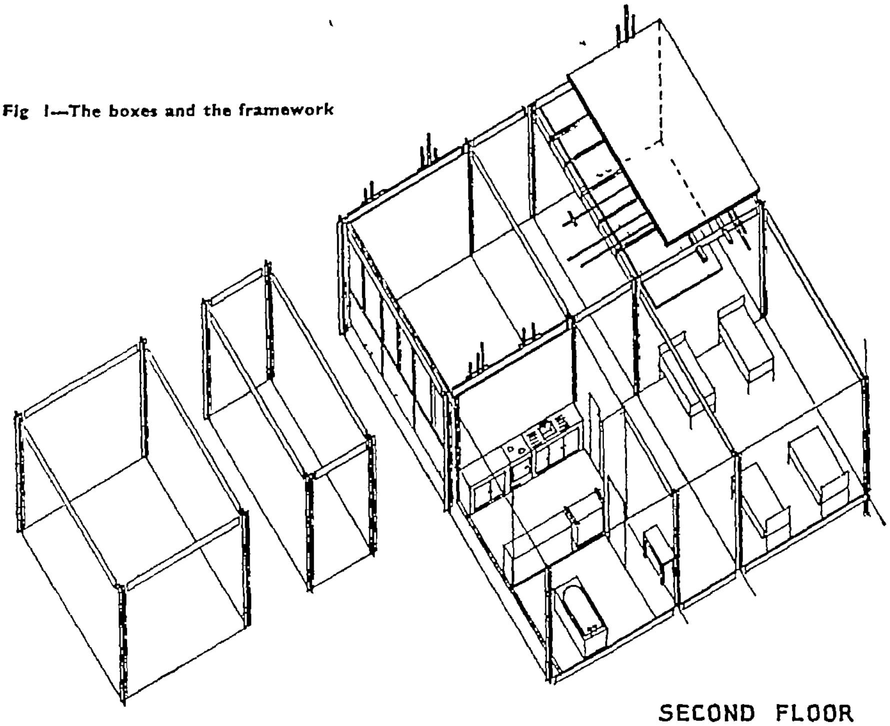

Fig 1—The boxes and the framework

fundamental change in what a school should be, whereas new hospitals must be very different from those we have built in the past

### Planning and Structure

The relationship between planning and structure is the key For example, one room may be 10 ft long and 6 ft 8 in wide, another 4 ft × 3 ft 4 in, so that the width of one is double that of the other If, moreover, the building which contains the rooms also includes two columns which are 20 ft (6 ft × 3 ft 4 in) apart then there is a clear relation between the dimensions of the rooms and the structure of the building This simple relationship is the basis of standardised modular planning and standardised structure which, with the careful economic use of prefabrication, can mean quick building at low cost

How can this fusion of planning and structure be adapted to hospitals and all the different types of room which make up so complex a building? The rooms can be classed in four ways

(1) Rooms of similar use and of similar size
(2) Rooms of different use of similar size
(3) Various small rooms
(4) Extra large rooms which are almost departments in themselves—e g, laundries, main kitchens, bulk stores, &c

Examining the dimensions concerned and the design of various types of hospital building for home and tropical use, it is clear that many rooms—for example, a 4-bedded ward—are very much the same in very different types of hospital, a sluice in a maternity ward is often the same size as one in a surgical ward, though the equipment in the two rooms may differ considerably, operating theatres are usually 400–430 sq ft in area, whether they are to be used for neurosurgical work in London or plaster work in the Far East So it should be possible to standardise the different types of rooms, and thus evolve a system of rooms the dimensions of which are related to one another on a modular basis The unit of this system will then be the unit on which the whole building is based Developing this simple plan, it is possible to have a series of standard rooms, rather like a set of boxes of different sizes, which are so related in size that they can be placed in any combination within a standard framework

Into this framework the equipment and services of the hospital must be fitted, with means for modifying the mains services as an integral part of the structure, so that changes in planning and equipment can take place without much interference with the working of the hospital as a whole The final result is a combination of (*a*) any chosen series of different types of standardised rooms, (*b*) a structural frame, and (*c*) service facilities—all on a standardised modular basis

### Some Details of Structure

I do not intend to deal wit the technical details involve but I must say something mo about the structural side of th combination During recent yea research has been directed to

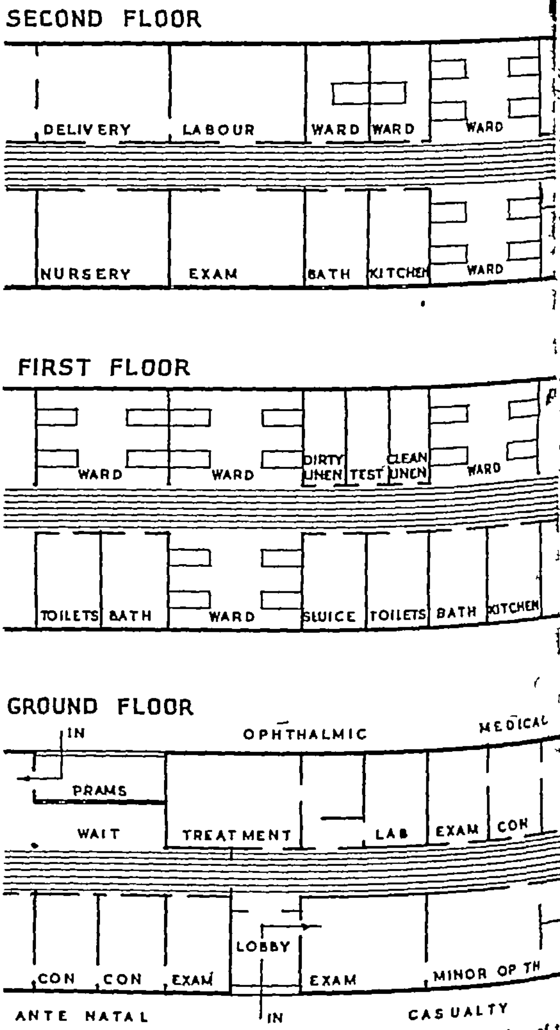

Fig 2—Section of a block, showing the vertical continuation of t ground-floor plan

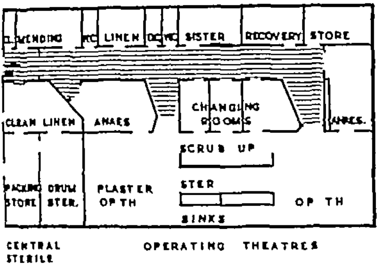

Fig. 1—An operating-theatre assembled from the basic units

ew form of building skeleton, light in weight economical produce and fulfilling the strength requirements of ditional types This skeleton is the outcome of a major velopment in the understanding of how building terials behave It is a very suitable form to incorporate standardised modular planning it can be quickly ected.

The structural frame can be visualised as composed of two ferent boxes; these can never vary in size but can be placed xt to one another in various combinations as partly shown fig. 1 Within each box a standard room, or combinations standard rooms, can be placed Where a very large room is quired this is formed by a series or combination of one or th of the two boxes

The standardisation gives a flexibility in planning that is th horizontal and vertical. Fig 2 shows a section of a block e ground floor of which is part of an outpatient department, e first floor a surgical ward, and the second floor a maternity rd and a delivery suite. This is not in any way intended a suggested arrangement of ward units but solely to illustrate how different rooms can be placed next to one another form departments and how these departments can be ered over one another thus achieving freedom in planning d flexibility in the placing of equipment There is no rigid n which cannot easily be changed to form another type unit with different room sizes and functions

Fig. 1 shows how an operating theatre and a central rilising department, as an example of a specialist unit, ght be assembled along these lines.

The design of the partitions are vital to the success of the sign. They are made of preplastered standard units of high ermal and sound insulation values, which can be put up ckly with the minimum of wet jointing (I consider that in ospitals partitions should not be dry jointed because with his method crevices are liable to develop ) The partitions are o designed that it is comparatively easy to move them if eed be.

Floors can be of one of several materials, for this is the sort f detail which varies according to function and climate for ample in this country today cork floors are often favoured r wards but in the Middle East cork is unsuitable because e temperature dries it up and in tropical as opposed to b-tropical regions, mosaic is often preferred Even anti atic operating theatre floors, of any given surface resistance n be incorporated in the system

The underside of the floor is formed by a sound absorbing ating which conforms to the general standards of hygiene; nd between the floor and the ceiling below run horizontal cts carrying mains services, which need no special fixing cause the fixing arrangements are part of the structure

The outside walls are in panels, being partly windows and partly walling The type of window varies according to the use of the rooms they serve For the tropics, special louvres with antiglare glass have been designed to fit the wall panels. An insulated wall is needed for the British climate but in hot countries different kinds of wall can be used depending on what local materials and skills are available

It is a simple matter to fix exterior panels into the structural frame and, for overseas work to erect antiglare baffles which allow cross-ventilation

### Estimated Saving

A hospital of about 300 beds was planned so that it could be compared accurately in cost with one of similar size designed on traditional lines The use of economical materials and the anticipated speed of erection made the estimated cost of the "modular" hospital 20% less than that of the hospital of traditional design To translate this into cash it may be estimated that a hospital of 300 beds in this country would cost about £900,000 In oversea work where economy (especially in the transport of materials) and man hours (particularly skilled man hours) are vital factors this reduction in probable cost should at least be maintained

* * *

This approach, relating hospital planning and construction to a module, also allows standardisation of detail so that the whole hospital can be built to the high quality of design that is of prime importance On the other hand the plan is flexible enough to dispel any fears of dull uniformity and 'standard' hospitals The methods I have outlined can I think do a great deal to get the new hospitals we need built in the reasonably near future

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## Special Articles

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### JOINT CONSULTANTS COMMITTEE

A MEETING of the Joint Consultants Committee was held on Jan 26 under the chairmanship of Sir Russell Brain when the committee was largely occupied in reviewing the progress of discussions with the Minister of Health and with officers of his department on a number of outstanding subjects

*Medical Advisory Machinery*

The committee welcomed the Minister's assurance that he sympathised with the committee's wish for close coöperation between hospital boards and their consultant staffs through the establishment of satisfactory medical advisory machinery, and noted his request for evidence of the unsatisfactory nature of the present arrangements. It was reported that the Central Consultants and Specialists Committee was endeavouring to obtain such information through its regional organisation. The committee felt that it would be helpful if it could be given an opportunity of discussing the problem with the chairmen of hospital boards and it decided to ask the Ministry whether this could be arranged.

*Development of Consultant Services*

Figures supplied to the committee by the [illegible] in the course of discussions on hospital [illegible] had given the committee some cause for [illegible] of balance between the estimated number of [illegible] sessions and the number of [illegible] in the various specialties It had [illegible] committee that there was a [illegible] overall planning of the consultant [illegible] country The committee's view had been [illegible] the Ministry which had expressed its [illegible] the committee on all aspects of the [illegible] Ministry's offer to [illegible] enable the committee [illegible]

*Provision of [illegible]*

At a previous [illegible] the Minister [illegible] had stressed [illegible] dation, and [illegible] with the [illegible] The [illegible] Minister [illegible] take [illegible] [illegible] decided that the question should be borne in mind for further discussion with the Ministry in connection with the forthcoming negotiations on hospital staffing

*Option for Whole time or Part-time Service*

It was reported that the Ministry had undertaken to consider the publication of an " agreed " statement in the medical press for the information of the profession on the granting to consultants of the option of whole time or part time service A draft statement which had been submitted to the Ministry for its approval was presented to the committee

*Domiciliary Consultation Arrangements*

The committee received a report from its subcommittee which, after discussions with representatives of the General Medical Services Committee, had urged upon the Ministry the desirability of an extension of the domiciliary consultation arrangements to patients in nursing homes The attention of the Ministry had been drawn to the hardship inflicted upon patients of modest means who entered nursing-homes for domestic reasons and because of the lack of adequate hospital accommodation, and were deprived of the benefit of consultant advice under the National Health Service

It was reported that, although the Ministry was considering the committee's proposal, its first reaction was that the Minister's statutory obligation to provide a domiciliary consultant service was specifically limited to the patient's home

*Appointment of Consultants and S H M O s*

A report was received upon the discussions with the Ministry regarding the procedure for the appointment of consultants and S H M O s The Ministry, while acknowledging that the existing procedure was open to criticism, had expressed its reluctance to amend the regulations if improvements could be achieved by administrative action It had asked the joint committee for specific suggestions so that the question could be studied further The matter was referred to a subcommittee for detailed consideration

*Other Matters*

Other matters discussed by the committee included the employment of hospital staff on pneumoconiosis medical panels, the recommendations of the Bradbeer Committee on hospital administration, the loan of hospital records to Government departments, and the possibility of arranging facilities for the interchange of registrars between the United Kingdom and countries overseas

## N H S SUPPLEMENTARY ESTIMATES

THIS year, for the first time since 1949–50, the Government has asked for a supplementary estimate[1] to meet the ordinary expenses of the National Health Service For England, Wales, and Scotland a further £6 million is needed to eke out the original estimate of £433 million Of the £6 million £4,848,000 is needed for England and Wales, and £1,233,000 for Scotland The supplementary estimates would be larger but for expected savings of £3 million scattered in small sums under many subheadings Chief of these expected savings is £1,209,000 on the hospital capital account in England and £651,000 on Civil Defence

Most of the extra money will go to the hospital boards to cover higher salaries and increased price of goods In England and Wales the boards will receive an additional £2,668,000, and in Scotland £987,000 There has also been a rise in the cost of the pharmaceutical and dental services The pharmaceutical services in England and Wales need a further £2,133,000, and in Scotland £250,000, and the dental services in England and Wales need £1,701,000, and in Scotland £200,000 The rise in cost of the pharmaceutical services is attributed to an increase the number and average cost of prescriptions, though in England and Wales this has been partly offset by th revised arrangements for pricing prescriptions and pay pharmacists The rise in the cost of the dental serv is due to increasing demand for treatment

# Medicine and the Law

## What is Negligence?

A MOST important judgment on the principles negligence has been given in the Scottish Court of Sess The court ordered a retrial in an action for damag brought by a Glasgow woman against a doctor[1]

She avers that the doctor negligently allowed a needle break when giving her an injection in November, 19 Despite a series of operations it has not been possible remove the fragment of the needle, and the plaintiff sues £2500 damages It is alleged that the type of needle was n strong enough, and that " any doctor possessing a fair average knowledge of his profession must have known th

The doctor maintains that the needle was suitable for t purpose and that it broke accidentally while he was w drawing it It was not uncommon for needles to bre without any lack of care on the part of the administrator

In July last a jury found unanimously for the doct The sole ground of appeal was misdirection of the j by the judge The judge had directed them that th must be such a departure from the normal and us practice of general practitioners as could reasonably described as gross negligence

The Court of Session has held that the direction d not accurately set out the legal criterion for liability, a therefore the jury's verdict could not stand The Lo President said that to succeed in an action based negligence, whether against a doctor or anyone else, was necessary to establish a breach of that duty to ta care which law required, and the degree of want of c which constituted negligence must vary with the circu stances But where the conduct of a doctor, or inde any professional man, was concerned, the circumstan were not so clear cut as in the normal case

*In the realm of diagnosis and treatment,* said his Lor ship, there was ample scope for genuine difference opinion, and one man was not negligent merely becau his conclusion differed from that of other profession men, nor because he had displayed less skill and kno ledge than others would have shown The true test negligence in diagnosis or treatment was whether t doctor had been proved guilty of such failure as doctor of ordinary skill would be guilty of if acting w ordinary care The standard seemed to be the same England

It was a tribute to the high standard of the medic profession in Scotland that there were practically decisions on that question in the reported cases But analogy was afforded by a series of decisions on allegatio of negligence against lawyers, in those cases me errors in interpreting the law or lack of knowledge of t law were not treated as constituting negligence several of those cases the words " gross negligence " we used His Lordship was not prepared to say that t concept of gross negligence formed no part of the law Scotland today, but in relation to professional negligen he regarded the phrase only as indicating so marked departure from the normal standard of conduct of professional man as to infer a lack of that ordinary ca which a man of ordinary skill would display So inte preted the words aptly described the sound criterion the matter, but they might give the impression that the were degrees of negligence

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[1] 1954–55 Supplementary Estimate Civil Estimates and Estimates for Revenue Departments H.M. Stationery Office Pp 140 5s

[1] *Glasgow Herald* Jan. 21, 1955 *Scotsman* Feb 5, 1955

# In England Now

*Running Commentary by Peripatetic Correspondents*

HE Chief of the local Fire Brigade wants to know t I am going to do about Mrs Wotherspoon For the nd time in six months his boys have left their darts dominoes to clatter over to the old cottage by the n; and, like me, he always keeps one eye on the ner With all that paraffin and methylated spirit the house the old girl is asking for trouble, he says, why don't I certify her? But it is not as easy as that.

rs. Wotherspoon is as sane as you or I will be at her e, and is positively brilliant when judged by local dards. She may read her papers a day late, but the ation in Formosa or the bank rate are none the worse that as topics to distract my attention from her umatoid arthritis. The stairs are getting steeper, d she chooses to spend most of the day upstairs ttering round the little three-roomed flat she has trived. After all, I did tell her that damp was bad r rheumatics and the ground floor rooms were wet.

The old front door is screwed up fast and she keeps the k door bolted. The sound advice of her girlhood ing never to let strange men into the house has n replaced in inviolable old age by a reluctance to be dered in her bed which is understandable in view of ent fashions. The voluminous notes on the back r allow the travelling vans *to supply her material* ds, but the chandler seems to be catching up on her e ground floor rooms are full of enamel bowls and ss jugs of paraffin pudding basins and jam jars are *pping trails of* meth over an equally generous stock of wood kindling It is not so bad upstairs, there are haps just three or four gallons of paraffin and a re intimate receptacle filled with meth After all, you live in the depths of the country in winter time must expect to be snowed up Look at the improvi nce of the people of Caithness, says Mrs. Wotherspoon, d she *for one is* not prepared to rely on aircraft-carriers helicopters passing her way by chance.

It is all very logical but Mrs. W's hand is getting her shaky and her eyes are not what they were. The stoves seem to be getting clumsier, the lamps are coming unsteadier every day The stuff is bound to spill if the funnel will not keep still, and tapers do t blow out like they used to in the old days Of course e does not want a fire any more than the people in the m next door, but they are thinking only of their cious hay barn and those stinking pigs. She has s a comfortable life interest in the late Mr Wother oon's estate, and a healthy distrust of the residuary tees' offers of hospitality She does not care a hoot at the coroner will say, and she is a staunch believer the hygienic advantages of cremation Perhaps it was cause Wotherspoon served the Empire faithfully for many years in India that his relict shows such com ure towards deferred suttee The Fire Chief and I d like having our fingers burned in the process

* * *

Those medieval healers whose appearances in market s were heralded by men beating on big drums, , clowns, and zanies were on to a good thing tably alone can cure many patients. The day after and as yet another of the legion of anonymous n on television my patients were all much better anxiety states were less tense, the obsessionals less lsive, the depressives more cheerful In their ons says they let me know that seeing me on the n had done them a lot of good Somehow I was a ter doctor after facing the cameras and they felt orally reassured. And one hysterical aphonia of g standing was cured immediately she saw my face set She shouted loud and clear to her mother, was upstairs: "Mum Mum, come quick and look y doctor on the Telly, and she has been talking y and vigorously ever since

Perhaps the answer to this vexed question of getting h doctors to cope with the ever increasing stream notic treatment-seekers is teleovideosuggestive otherapy

* * *

I wonder whether your peripatetic cat-fanciers could help with our problem For two years our household has been ruled by a couple of alley type cats, and as we are expecting our first two legged addition to the family we feel there is bound to be a certain dislocation of the feline nose. We should welcome advice on what form this syndrome is likely to take Should we expect a reversion to box wetting and claw biting? Already the dis appearing lap is causing annoyance and the occupant is liable to vacate in panic with fœtal movements felt. However, they have happily appropriated the new cot, so I suppose the box in front of the boiler will have to be decorated with pink ribbon

* * *

My husband and I had just arrived in the tropics, and we were enjoying our first cocktail party Standing among the gay illuminations in our host's garden, I could not help but overhear the advice being given to my husband.

' *You must first decide whether you are going to be a sand man or a sawdust man.*

I have never seen such a canopy of stars; shining clearly in the darkening sky they resembled lamps hanging down from Heaven. The sickle moon was slowly setting in the west, not bright enough to dwarf the stellar radiance but matching the brilliance of the planet Jupiter as a fellow member of the solar comity

*You must do your best to keep the contents dry'*

The frangipani trees hold aloft their flowers with thick succulent branches They moved little in the cool, refreshing breeze with an air of stern, reproving majesty

' *A common mistake is to make the hole too small—make it larger than you think you'll need it and you won't regret it*

The poinsettias swayed and danced in the fairy lights, their colours matching the ladies frocks and adding an enchanted elegance to the occasion Their redness stood out brightly in the evening light, while their yellow tints were subdued and suppressed.

*And make sure the edge is smooth and rounded There is nothing so uncomfortable as a sharp square edge."*

The poison tree had not been watered and was a bank of colour This teeming radiance without a single leaf was attractive and alluring A poison tree indeed—better by far a garland tree, a bouquet-tree, a barbola tree

' *See that the lid is hinged so that you can have a good look round underneath One doesn't mind a few ants but if a scorpion is there you want to see it first*

The stars were superb The frangipani trees, the poinsettias the poison tree were out of fairy tales. But how different Khartoum will be when it has water sanitation.

* * *

Some decry the football pools, but recently I had reason to be glad of the knowledge gained as a regular investor by my working partner on the C.P.H. course

We had been set some problems in medical statistics to illustrate use of the binomial expansion: $(a+b)^2 = a^2+2ab+b^2$ $(a+b)^3 = a^3+3ab^2+3a^2b+b^3$, etc This can be used as a method of finding expected mortality rates in samples of given size. When we came to $(a+b)^{12} = a^{12}+12ab^{11}+66a^2b^{10}+220a^3b^9$ , the working out of the integral numbers 12 66, 220 threatened to be an irksome business for two mediocre arithmeticians Happily my partner spotted early on that these numbers represented: number of possible ones in 12 number of possible twos in 12, number of possible threes in 12, etc.—information which he used weekly in his treble-chance permutations. Many of the numbers of the series he had off by heart from long use Those he did not already know we found by reference to a small publication he happened to have in his pocket, *Popular Permutations for Punters.*

* * *

*Notes from Madeira*—"The hotel garden contains 1 ♀ peacock, and 2♂ 2 dogs (spotted), 1 dog (plain), and 3 cats. Curiously enough our Portuguese phrase-book does not contain the only phrase wanted so far at a small grocer's: I want some of those nuts. They look disgusting but they're only for the peacocks.'

# Letters to the Editor

## FAULTY DETOXICATION IN SCHIZOPHRENIA

SIR,—Quastel and Wales[1,2] showed that in catatonic forms of schizophrenia hippuric-acid excretion is lowered after administration of sodium benzoate Others[3,4] have confirmed these results and extended them to other schizophrenic conditions Various explanations were later suggested for this "faulty detoxication" in schizophrenia[3,5–7]

Our present knowledge indicates that the formation of hippuric acid requires the conjugation of glycine and benzoate in the presence of adenosine triphosphate, magnesium ions, and coenzyme A[8–10] In some acute schizophrenics we have found high amounts of glycine in the early morning urine (e g, 90 µg per mg creatinine, as measured by quantitative paper chromatography) These patients had a low hippuric acid excretion (approximately 2 g) during the four hours after the subsequent oral administration of 6 g of sodium benzoate, the amount of glycine in this urine was substantially diminished compared with the glycine in the early morning specimen

Partial starvation, high protein katabolism,[5] decreased thyroid function[11–13] (which is believed to be connected with the regulation of the coenzyme A level[9]), and decreased basal metabolic rate[5] seem to be among the factors involved in this inverse relationship

Simultaneous administration of sodium benzoate and a surplus of glycine raises significantly the excretion of hippuric acid in certain schizophrenics, but only slightly in normal people[3] A surplus of substrate, however, could raise the concentration of its enzyme, hence it is likely that decreased conjugation (utilisation) of glycine prevails during those phases of the schizophrenic process which are characterised by a low hippuric acid test

The urinary glycine of normal people we found to be higher during the night (40–80 µg per mg creatinine) than in the morning (30–50 µg per mg creatinine) These values were also inversely related to the hippuric acid values in normal persons after ingestion of sodium benzoate which we had found earlier to be about 10% lower during the night than in the morning[4]

These and other data[5,14–16] have led us to regard the metabolic pattern of healthy people during the night as equivalent to the metabolic pattern of certain schizophrenics during the daytime, such a change in the diurnal rhythm suggests new lines of research in schizophrenia A detailed account of our method and data is to be published elsewhere

These studies were made under the direction of the Saskatchewan Committee on schizophrenia research, and supported by the Department of National Health and Welfare, Ottawa, and by the Rockefeller Foundation, New York We are indebted to Dr Ian Clancey and Dr J Lucy, clinical directors, Dr J Stephen, director of laboratories, and Miss Helen Keay for their help

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ALLAN TREW
ROLAND FISCHER.

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3 Georgi F Fischer R. Weber, R Weis P *Schweiz med Wschr* 1948 78, 1144
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## SANATORIA

SIR,—Sanatoria have performed a great service to th community and it is with regret that one sees the pas of such a world-famous institution as the Trude Sanatorium Yet this must be only the beginning of long series of inevitable closures unless these institutio are diverted to other work—a trend already obvious certain sanatoria in the London area where non tuberc lous thoracic surgery is now commonplace

It is not only "declining morbidity" and the adve of chemotherapy which has produced the present low rate of admission to sanatoria the increasing use domiciliary management of patients, so successful at time when sanatorium beds were at a premium, plays part Experiments with ambulant chemothera mentioned by Dr Pritchard (Feb 5), are a logical st forward, particularly for early cases of doubtful activ and "chronics" (Paradoxically, however, reliable tri of such methods would probably be best carried out sanatoria where controlled conditions could be obtaine

One is on more debatable ground with the ill patie Is such a patient to enter sanatorium? I feel that integrated scheme managed entirely from the ch clinic ("clinic management") would make this unne sary Such a scheme must include local hospital b with thoracic surgical facilities, a well organised do ciliary service, and provision for ambulant chemothera This has positive advantages over sanatorium admiss

The patient and his family remain under the care of physician and his team throughout the period of managem —a factor of vital importance in a long term illness invol many social and psychological factors (not to mention di ences in clinical opinion!) The whole of the treatmen managed *locally*, permitting daily visits by relatives patients in hospital (most important for contented coöperation, and good morale) The segregation of the pa in a distant institution, which houses only "T.B" sufferers is remote from civilisation, increases the sense of sti which, all too frequently, afflicts the tuberculous pati This is largely avoided in clinic management, for contact the outside world is maintained Sufferers from other illn are treated in the same hospital and patients who are bac work are met at the clinic Under these conditions patient's outlook remains more normal and his return employment needs less psychological readjustment

What will be the long term clinical results of such schem A recent five year follow up of 64 patients managed Hammersmith Chest Clinic in the pre chemotherapy and with much simpler facilities than those now availa reveals a most encouraging picture 100% survival and 10 quiescence for 12 B1 cases, 93% survival and 70% quiesc for 41 B2 cases, 82% survival and 64% quiescence for B3 cases Satisfactory as these figures are, further impr ment can confidently be expected with modern chemother

Finally, the possible danger of infection in hospital home should be mentioned because it has been gro exaggerated, particularly recently in relation to gene hospital admission There is no greater danger of infect in a well run hospital containing tuberculosis wards than one without them In fact there is an advantage, for pati in the general wards, found to have tuberculosis, can promptly transferred to the tuberculosis unit where spe nursing precautions are taken[2] Good living standards, B vaccination, and adequate medical supervision of the nur staff reduce the danger to minimal levels[3] Infection in home can also be combated once the source case is diagno and appropriate action taken This depends chiefly adequate instruction in hygiene,[4] including effective sputu disposal methods[5]

I cannot agree with Mr Temple (Jan 8) that it wo be a wise investment to rebuild some of the sanato

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1 Stradling P *Tubercle* 1955 (in the press)
2 Ball K P Joules, H Toussaint C H C Heady J A *Lan* 1950 ii 121
3 Simmonds F A H The Protection of the Nurse Against Tub culosis National Association for the Prevention of Tubercul London, 1952
4 Grenville Mathers R Trenchard H J *Proc. R. Soc M* 1953, 46 809
5 Stradling P *Lancet*, 1953 ii, 1185

er much one may regret the passing of the ium, the steady reduction of the disease to which its existence is bound to favour this trend hile we have an effective substitute in a chest ervice and its related hospital beds forming a k over the country Great improvement of this service of preventive methods and early diag hould form the basis of an all out drive against llosis, needed even more now that eradication is able

ersmith Chest Clinic
London, W 1*　　PETER STRADLING

## HE FAMILY IN THE MODERN WORLD

—It was interesting to read the condensed version 5) of Dr Henry Dicks's valuable paper on the ment of the family in the modern world with the us on the harmful effect of modern urban nalisation and housing

prevalence of the neuroses and psychosomatic among relatively young people is only too obvious must be a reflection in considerable measure of rest and instability in the lives of many families. we can really censure urban *industrialisation* for than a small share of this, and are Dr Dicks's term recommendations anything more than hopeful ing?

rely the well being happiness, and stability of the ly are largely dependent on the influence of the her She should be the unobtrusive centre and erstone around which the whole unit revolves and lives May I ask what training she receives for this ly difficult, anxious, and onerous task?

n we not lay the blame squarely on the shoulders ur educationalists for failing to train and prepare young girl for her vital life's work as a wife and ther? Is not the present schoolgirls curriculum eiously ill fitted and ill adapted for the important es which most of them will have to fulfil in their are lives? It would be a pleasant and revealing task design a suitable syllabus but I am not aware that men are usually accepted as educationalists

bruge　　JOHN ROBERTS

## CYCLICAL VOMITING

Sir,—I was interested by the reference to 2 cases of ical vomiting as 'masked epilepsy' in the article Dr Wallis in your issue of Jan 8

At the annual meeting of the Western Society for diatric Research held in Los Angeles on Nov 20 54 I presented a paper entitled 'cyclic vomiting a m of epilepsy in children' (part of an article in the ss¹). The evidence that this symptom complex and er associated periodic disorders of childhood, may be garded as examples of autonomic epilepsy was obtained m a study of 33 children. In all patients a diagnosis of lical vomiting had been made following careful ical studies to exclude intrinsic disease of abdominal d other viscera The vomiting was periodic in type d of prolonged duration it was associated with ever and frequently with dehydration A history of d mal or psychomotor epilepsy was obtained in 7 ents whose clinical features were similar to those with mplicated cyclical vomiting There was a family ory of epilepsy in 5 children (15%) 2 of whom were ressed to grand mal seizures Evidence of acquired ain injury was present in 14 patients (42%) a similar ber having persistent vomiting or feeding difficulty er colic and rumination during infancy Episodic ptoms apart from vomiting were abdominal pain dache behaviour disorder fever skin rash, and b pain. The electro-encephalogram was abnormal in 2 patients, and seizure discharges, which occurred in 76% included focal abnormalities, predominantly in the temporal leads Phenytoin sodium was the most effective anticonvulsant for the prevention of attacks and pheno barbitone or suppositories of ergotamine tartrate and caffeine were of value *in their alleviation*

Cyclical vomiting, in each of these patients was classed as an epilepsy of the autonomic type The three main criteria which favour this diagnosis are (1) recurrent and paroxysmal nature of attacks (2) absence of intrinsic disease of abdominal and other viscera and (3) positive evidence of cerebral dysfunction as manifested by a personal or family history of epilepsy including migraine a history of acquired brain damage, abnormal neurological signs E.E.G abnormalities, and a beneficial response to anti epileptic drugs With the recognition of a cerebral origin for cyclical vomiting and other periodic disorders the child may be released from prolonged and repeated investigation and the seizures prevented by regular anticonvulsant medication

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[1] Millichap J G, Lombroso C Lennox W G (in the press)

## LUNGS, BONES, AND JOINTS

SIR —Your annotation last week on this subject is of special concern to those like myself interested in the relationship between joint and lung lesions In 1947[1] I drew attention to fully developed Bamberger Marie's disease with its soft tissue bone and joint swellings —"hypertrophic pulmonary osteo arthropathy"—occurring as a presenting feature in some cases of bronchial carcinoma Indeed in some of these cases the arthritic manifestations of rheumatoid disease, the so-called rheumatoid arthritis had been diagnosed and treated as such for several months and yet in none were there symptoms referable to the chest

Your annotation fails to stress the remarkable response of such joint lesions to lung resection when within a day or two complete reversion from crippledom is achieved Patients totally dependent in daily life become self supporting overnight

Opening a discussion on unusual manifestations of bronchial carcinoma at the section of medicine at the Royal Society of Medicine,[2] I described 6 cases from a series of 200 consecutive cases of bronchial carcinoma who presented with joint manifestations in the form of an acute or chronic polyarthritis as the initial complaint In none was there any real evidence of extensive tissue breakdown or appreciable infection and the association of the joint and lung conditions on the basis of infection alone or of anoxia is difficult to explain

The possible association of acromegaly and pulmonary osteo arthropathy noted by Fried[3] *occurred in 2 of* my cases with acromegalic features Large spade like hands the increased size of the bones due to periosteal reactions swollen joints increased soft-tissue swellings with clubbed fingers and a 'clubbed nose' occurred in 2 of my cases.

The dramatic *response* of *these swellings* to lung resection would certainly suggest that the causative factor arises from within the lung Crump[4] incriminates an abnormal substance circulating in the blood and producing these bone joint and soft-tissue swellings and Aschoff[5] *suggests that the lungs* pulmonary glands take on additional functions as secreting organs

The few cases of pleural mesothelioma that I have seen have not shown arthropathic manifestations, and I question to what extent the pleura is involved in the osteo-arthropathy The *observations* of Ray and Fisher[6]

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1 Ellman, P *Lancet* 1947 1, 464
2 Ellman P *Proc R Soc Med* 1953, 46, 851
3. Fried, B M. Bronchogenic Carcinoma and Adenoma London, 1948; p 60
4 Crump C *Virchows Arch* 1929 271 467
5 Aschoff L. *Z ges exp Med* 1926 50 51
6 Ray E. S., Fisher H P *Ann intern Med* 1953 38 239

that the tumour was located peripherally in 13 of their 14 cases is of considerable interest They indicated that neither the size of the tumour nor the type of malignant cells played any apparent rôle in the pathogenesis of the osteo arthropathy

Finally, these joint/lung lesions must be distinguished from "rheumatoid lung disease" which is of two patterns (1) interstitial lung involvement occurring with joint lesions as systemic manifestations of "rheumatoid disease" [7,8], and (2) serous-membrane involvement with rheumatoid nodules wherein the lung and pleura (the latter more commonly) may be studded with rheumatoid nodules with histological features resembling the subcutaneous rheumatoid nodule [9,10] In 1 of Christie's 3 cases the rheumatoid necrotic nodule occupied the whole of the right upper lobe In the light of your annotation it is not without interest that the "pleural nodules" were associated purely with rheumatoid joint lesions and not with pulmonary osteo arthropathy

London, W 1 **PHILIP ELLMAN**

## TREATMENT OF IMPETIGO

SIR,—I chose to use 'Graneodin' for the same reasons as Dr McMaster (Feb 5) I, too, over a period of two or three months, have been using it in impetigo, and I am most satisfied with the rapidity of cure and ease of application My conscience as a producer of aureomycin-resistant staphylococci is kept clear, and the patients are cured—so everybody is well served

London E 2 **G G LAWSON**

## PSYCHOLOGICAL ASPECTS OF UTERINE DYSFUNCTION

SIR,—We found Dr Cramond's paper in your issue of Dec 18 particularly interesting as we were members of a team working on this problem in 1950 Both studies should, in our opinion, be regarded merely as preliminary studies in which even the field of investigation is not yet adequately defined Dr Cramond's paper begins to dispose of many of the ætiological myths current in psychological medicine We would not ourselves have regarded any one of these factors as being significant We have also found that women who showed obvious overt anxiety during pregnancy would, after reassurance, have an average labour, the uterine dysfunction group, on the contrary, tended to be rigid, overconscientious, and inaccessible In fact, access to the most significant contradictions in their lives could be obtained only after several psychiatric interviews

Dr Cramond's paper was disappointing, however, in that he did not state in how many of the labours in his group the length was over 48 hours We ourselves felt, after examining the records of a similar-sized group with controls, that the patients who were most interesting were those who had recorded labours of more than 48 hours The onset of labour is notoriously difficult to determine We would also have liked to know how many of his dysfunction group had other obstetric abnormalities, since all were delivered by forceps or cæsarean section In 1951, after increasing our operative interference as a matter of policy, 30% of patients whose labour lasted more than 48 hours delivered themselves spontaneously

We would also like more information as to the nature of the antenatal education offered to Dr Cramond's patients, before dismissing this matter so lightly We have found that a carefully designed "natural childbirth" programme does not operate primarily through the classes, on the contrary, after a period of years it operates most strongly in the labour ward, where all patients are affected whether they have attended classes or not It was in this context that the figures "cite by Mandy" were originally given by one of us. D Cramond does not describe the labour-ward manageme of his patients

The findings of our team were summarised [1] as follow

> "Granted the sort of patient who is relatively inferti tends to grow a big baby, has a long hard 'sacral' cerv and an occipito posterior presentation, add to this the ty of psychological make up which reacts to adversity with la of insight, depression and a state of tension, add also mar and general social stress then long labour is more likely th if these factors were not coincident"

This statement contradicts Dr. Cramond's view th prediction is not possible, it actually shows that pr diction requires the close coöperation of a team interest antenatally in more than the purely mechanical

Obstetric Hospital
University College Hospital,
London, W C 1

**ELIZABETH TYLDE**
**W C W NIXON**
**SHILA G RANSOM**

## ÆTIOLOGY OF PREGNANCY TOXÆMIA

SIR,—In showing that blood flow through the uter wall is reduced in cases of pre eclampsia, Mr Mor and his colleagues (Feb 12, p 323) have made a m valuable contribution to our knowledge of the fact giving rise to this disorder

There was already evidence from which this find could be predicted

Browne and Veall [2] demonstrated that in cases of toxæ there is relative placental ischæmia, and, unless there also uterine ischæmia, one would expect the associated hyp tension to cause uterine hyperæmia—which it does n The placental ischæmia can in fact be most easily regar as a consequence of the reduction of the flow of blood thro the uterine wall Again, Reynolds [3,4] showed that tens in the uterine muscle reduces circulation through the ute wall and that this enhanced tension is reflected by the uter outline in first pregnancies and especially in toxæmia

The University College Hospital workers give further confirmation of the association of myometr ischæmia and the toxæmic state, and by citing Bek Bastiaanse, and Page they subscribe to the view that t ischæmia is caused by the heightened tension of t uterine muscle I cannot, however, agree with th hypothesis that the resulting trophoblastic anoxæ is an important factor in the ætiology The occurrenc of postpartum eclampsia, and the recurrence of eclamps during labour after toxæmia has abated because of th death of the fœtus in utero, is proof to the contrary N is their evidence of impaired trophoblastic metabolis unchallengeable

The data that Venning, Singer, and Simpson offer cann be set forth in logical propositions "For it is seen that wh the formaldehydogenic steroids showed a marked increa in both mild and moderate toxæmia over their amounts normal pregnancy, there occurred (surprisingly) a sha decline—even to levels below that found in the health pregnant—in severe pre eclamptic states" [5]

Contrary to Ahlmark, whom they quote, Kapelle Adler [6,7] has found a considerable reduction of hist minase activity in pre eclamptic toxæmia, wh Gabwray [8] found no significant difference in the tot amount of conjugated and free histamine excreted pe day in the urine in normal pregnancy and in eclamps

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7 Ellman, P *Proc R Soc Med* 1947 40 332
8 Ellman P, Ball R E *Brit med J* 1948 ii, 817
9 Christie G S *Aust Ann Med* 1954, 1 49
10 Ellman P, Cudkowicz, L, Elwood, J S *J clin Path* 1954 7 239

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1 Nixon W C W *J Obstet Gynæc Brit Emp* 1952 59 6
2 Browne J C Veall N *Ibid* 1953 60 142
3 Reynolds S R M Physiology of the Uterus New Yor 1950 p 336 et seq
4 Reynolds S R M Baker, J T *Contr Embryol Carn Instn* 1951, 34 Publ 592
5 Sophian J *Amer J Obstet Gynec* 1954 68 733
6 Kapeller Adler R. Ciba Foundation Symposium on Toxæmi of Pregnancy London 1949
7 Kapeller Adler, R. *Int physiol Congr Copenhagen*, 1950 p 289
8 Gabwray B Anrep, G V Barsoum C S *Ibid*, p 212

he work of Smith and Smith has been considerably criticised. I have attempted a summary of this criticism [9] Marran [10] has stated that he does not find evidence degradation products of œstrin such as described Smith and Smith nor does he find pregnanediol ciencies in the majority of cases of toxæmia Support the view that trophoblastic metabolism is impaired t available in these directions.

r Morris and his colleagues seem to hint at a second on for the ischæmia of the uterus when they attribute reduced myometrial circulation to hypertension y cite the beneficial effect of rest and of hypotensive s but overlook the fact that these measures are ted against the renal ischæmia which they help overcome [11]

he work of Franklin [12] and Sophian [11] has shown that sistance to stretch of the uterus, which is accom ied by a myometrial ischæmia provokes a renal tical ischæmia and a renal blood flow diversion ch, to my mind can account for all the symptoms pre-eclamptic toxæmia This is not to deny that pertension can aggravate the myometrial ischæmia, to emphasise that such effect is merely a superadded

don, W 1 JOHN SOPHIAN

## MENTAL HEALTH AND PUBLIC HEALTH

ir,—In order to promote the mental health aspect the public health service, as recommended in your ing article of Jan 15, it would surely be necessary the public-health service to be extended to include age-groups of both sexes The public health service present completely unrepresentative of the public whole and, as mental health is an attribute of ilies and groups as much as of individuals, it seems me that very little permanent benefit will result the entire population is included.

lso, although we are all very conscious of our minds at st, the classical medical examination which concentrates the body if performed at routine intervals on the general lation, might by preventing disease of the body ease the individual and the public mind

ople fortunately do not like to think that they are ill ely to be ill in mind or body; and this prevents them seeking advice in the very earliest stages of illness, n the cost of treating them would be minimal; if medical ures were expended on this development in the public lth service and periodic medical examination was offered eryone—not only to mothers babies, and school-children rs—it would gradually be accepted by the public and ared by the medical profession. The improvement in mal health—already manifest in mothers and children— uces if adults are left to face the stresses of life with further regular medical supervision. Obviously this cannot ade compulsory but the psychologists could surely think way to make it acceptable

ld, Middlesex C M SMALL.

ir,—It is perhaps not fully realised that in many as the infant welfare and school clinics are already e concerned with problems of mental health than h physical ills Many mothers ask for advice on aviour at the infant welfare clinic and at routine ool medical examinations, and an increasing reluc e to encroach on the preserves of the general prac ner has given the assistant medical officer more time meet these demands In many areas a mental health vice has in fact been established and there is often ful liaison with schools. It is anomalous however the medical officers are for the most part untrained is field. It seems to me that the next step towards the provision of an effective service is not one of reorganisation but the equipment of medical personnel with knowledge of this specialty

Bexley S M RING
Assistant medical officer Kent.

## OSTEO-ARTHRITIS OF LUSCHKA JOINTS

SIR,—Professor Cave and his colleagues, in their valuable paper of Jan 22 rightly point out the importance of the Luschka joints in the ætiology of cervico brachial neuritis They make timely criticism of the fashionable and somewhat uncritical tendency in many quarters to ascribe all cases of cervico brachial neuritis to protrusion of a cervical intervertebral disc

I would, however, strongly disagree with their rather dogmatic statement that neck traction and manipulation are useless in this condition Much of the pain and stiffness in osteo arthritic joints is surely due to capsular scarring which may involve adjacent ligaments and tendons and to muscular spasm, rather than to pressure by osteophytes per se

A simple example will make this clear In many cases of osteo-arthritis of the hip in which X ray examination shows many osteophytes, careful manipulation under anæsthesia may increase the range of movement to a surprising degree showing that the limitation of movement previously present was not in fact due to the osteophytes but to the other factors I have mentioned

Incidentally the increased range of movement obtained thus by manipulation often helps the patient considerably The same principle applies to osteo arthritic joints generally including the cervical spine Hence the improvement that may follow both traction and manipulation in this region in carefully selected cases, granted obviously the necessary experience in the art of manipulation

London W 1 A G TIMBRELL FISHER

## FEMORAL HERNIA

SIR —Owing to the real or apparent prevalence of hernia in tropical Africa any correspondence on this subject is of interest here in Nigeria In his letter of Jan 8 Mr Pearce suggests the superiority of a McEvedy type operation for femoral hernia

In my practice, hernia occupies a very prominent position Inguinal hernia is, of course, far more frequent than femoral hernia, but it is precisely because of this that an approach which avoids the inguinal canal is desirable. When one is confronted day after day with inguinal and scrotal masses of all sizes and shapes and in varying stages of reducibility, one hesitates to mutilate the intact inguinal canal for the repair of a femoral hernia with the resulting tendency to inguinal hernia.

Approach to the sac may be varied I have found that a transverse suprapubic incision with division of the rectus sheath and retraction of the rectus muscle gives excellent exposure and leaves a strong and agreeably concealed scar As regards the peritoneum, I prefer to err on the side of opening it for inspection. In most cases this is unnecessary and will not be done In any case if manipulation is avoided a purse-string suture leaves negligible internal scarring In cases of incarceration or strangulation it is my custom to open the sac by a small separate incision over the swelling in the femoral triangle to allow the escape of transudate

I disagree with Mr Pearce on the necessity for closing the upper end of the femoral canal This brings me to an interesting point. It is my custom to close the canal with one or two unabsorbable sutures Unlike Mr. Pearce I have seen a hæmatoma form in the thigh on several occasions Perhaps this is because the herniæ here are often larger than those seen in Britain On the other hand is it possible that the closing of the femoral canal prevents the escape of blood or exudate? In all cases the fluid has eventually become absorbed but, as my patients have a lively critical sense it is not at all easy to reassure them of this and their confidence is

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J Toxæmias of Pregnancy London 1953; p 111
G. F Lecture at Postgraduate Medical School of 1915
J J Obstet. Gynæc., Brit Emp 1955 62, no 1
K. J Ibid

usually shaken if any swelling remains I have considered the possibility of this hæmatoma to be so real that in many cases I place a firm pad over the femoral triangle and rely on diligent supervision of exercise to ward off thrombosis So far we have had no cause for alarm

Catholic Mission Hospital,
Adazi Southern Nigeria
T F McELLIGOTT

## ELECTROLYTE DEPLETION IN PYLORIC STENOSIS

SIR,—I read with interest your annotation (Jan 8) on this subject

From observations on several patients with this condition, I would emphasise that the main disturbance comprises both fluid and electrolyte loss, and of the depleted electrolytes we consider potassium the most important The clinical picture in such a case closely resembles that of a myocardial lesion, and electrocardiography shows a flattened T wave, as a result of potassium depletion This is a temporary alteration, which is quickly relieved by administration of potassium salt, after which the T wave reverts to normal But although we regard potassium loss as one of the most important disturbances, we cannot neglect chloride and sodium requirements Infusion of saline solution leads to temporary recovery, with rehydration and a rising blood-pressure, even without the addition of potassium

I would therefore emphasise that in pyloric stenosis there is a need for both fluids and electrolytes, and of the electrolytes potassium is the most important to avert cardiac disturbance Lasting improvement is to be expected from operation

III Internal Clinic,
Belgrade
M ANDREJEVIĆ

## TREATMENT OF HYPERTENSION

SIR,—I was interested to read the paper by Dr Ashby and his colleagues (Jan 29) Perhaps I have been unlucky, but I have been discouraged from using oral pentolinium tartrate because 2 of my patients have had severe hypotensive crises due, I think, to the drug

The first, a woman of 49, was at the time in hospital whilst the appropriate dose was being determined Whilst on 'Ansolysen' (80 mg at 8 A M, 2 P M, and 8 P M) she developed colicky abdominal pain and constipation, for which she was given an enema Shortly afterwards she collapsed, but in the course of half an hour or so she recovered It seemed likely that her collapse was due to sudden absorption of the drug from the large bowel precipitated by rendering the bowel contents fluid

The other patient, a woman of 50, had a fairly well stabilised blood pressure on ansolysen by mouth (120 mg at 7 30 A M, 40 mg at 1 P M, 120 mg at 3 30 P M, and 40 mg at 11 P M), and had been on this dose for about four months when, at about 10 30 A M one morning, she felt faint and actually lost consciousness for ten minutes Her husband, a pharmaceutical chemist, said that she became extremely pale an pulseless She recovered fully in an hour or so and cook the Sunday dinner ! The patient had never fainted befor

In view of these two alarms I have abandoned the u of powerful ganglion blocking agents by mouth, a control severe hypertension with 'Serpasil' by mou with the addition, if necessary, of subcutaneous ansoly retard injections self administered twice a day (usual in the early morning and in the afternoon)

I have just reviewed cases that I have treated in rece years and the accompanying table shows the resu achieved with various forms of treatment

Wrexham
P R C EVANS

## TOO MANY ANTIPYRETICS?

SIR,—Dr Sherwood (Feb 5) says that Dr Brons (Jan 29) is wrong in saying that his pyrexia deals w pathogens, and that the good work is done by antibodies

It seems that fever can occur in many diseases with the presence of a discoverable pathogen—e g, in ac rheumatism, where it appears to be part of an alle response to toxin(s) However, there is another kin case in which fever may be provoked by a diffe mechanism which I have long believed to be m important than antibodies

I may not be original in this—I do not know I sug that micro organisms pathogenic to man in general g best at or about normal human body temperature and elevation of temperature is an attempt by the body w attacked by a pathogen to produce conditions unfavour for the invader If this view be correct, then febrile resp to infection not only is not "an incidental reaction of the to the parasite" but has been responsible for the surviv date of the human race and of all other warm blooded lif

The discussion of "antipyretics" cannot go much fur without a definition of their nature and of the type of suitable for their use I suggest that by antipyretic drug mean what we say but tacitly exclude chemotherapeutic antibacterial drugs If this be agreed, then antipyretics h their place only in febrile illnesses of unknown or perhaps v origin or in those cases in which chemotherapy is not indic or has failed

Gaillimh Ireland
SEAGHĀN UA CONCHUBHAI

SIR,—I was interested in Dr Sherwood's views pyrexia in illness He states that antibodies dealt w my infection and not the pyrexia I think few will w to quarrel with that I shall continue to believe, h ever, that the production and function of antibodie not interfered with (and may well be accelerated) dur a fever, until I learn of evidence to the contrary

London S E 9
N P BRONSDO

TREATMENT OF HYPERTENSION

| Drug | Labile hypertension | | | Essential hypertension (1 case of ! pyelonephritis) | | | Malignant hypertension | | | Chronic nephritis | | | All groups | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Good | Fair | Poor | Good | Fair | Poor | Good | Fair | Poor | Good | Fair | Poor | Good | Fair | P |
| 'Ansolysen Retard' or Vegolysen Retard or hexamethonium bromide in dextran | | | | 6* | 3 | 1 | 1 | 4 | | | 1 | | 7 | 8 | |
| 'Ansolysen Retard + Serpasil | | | | 1 | | | 2 | 2 | | 1 | | | 4 | 2 | |
| 'Serpasil | 1 | | | 2 | 2 | | | | | | | | 3 | 2 | |
| Ansolysen by mouth or Vegolysen' by mouth | 1 | | | 4† | 2 | | | | | | | | 5 | 2 | |
| 'Ansolysen' by injection or Vegolysen by injection | | | | | 1 | 3 | | 1 | 1‡ | | | 1‡ | | 2 | |

* 1 patient became hypersensitive to dextran † 2 patients had severe reactions ‡ Uræmia on admission patient died
Good = Blood pressure kept within normal limits most of the time when patient up and about and seen as an outpatient.
Fair = Appreciable reduction in blood pressure but still raised above normal
Poor = No appreciable reduction in blood pressure

## REINFORCING PLASTER-OF-PARIS

—I have read with interest the letter by Mr …as in your issue of Jan 22, and I think there is a need for lighter plaster casts to relieve the burden …ose patients who have to wear spinal jackets or …ecas.

…e combination of a plaster with Glassona, which …e been using for the last three or four years …ly lightens their load and enables them to get up …walk with much greater ease than they have been …to do in the heavier conventional plaster

…ssona alone, which tends to wrinkle and is slow …tting, is difficult to apply without a foundation …aster-of paris These disadvantages are overcome …a very thin foundation of 'Gypsona' is applied …padding and then strengthened by a few layers of …

…, Bristol, 8. KENNETH H PRIDIE

## …OURCE OF TUBERCULOUS INFECTION IN CHILDREN

—The excellent paper by Professor Illingworth and …lleagues (Feb 5) should be read by all interested in …evention of tuberculosis. May I draw special …tion to some statements on notification

…ny tuberculous persons—children and adults—are not …ed. Cases of tuberculous cervical adenitis or of tuber… of the kidney bones, or joints are particularly liable …left unnotified A positive tuberculin reaction as the …vidence of tuberculous disease is not acceptable to the …as a reason for notification although it is obvious …e notification of young children with a positive tuber… …action may well lead to the discovery of an open case …rculous There would seem to be good grounds for …ing a modified form of notification, which would not …the patient to any possible disadvantages and yet …allow the chest physician to examine for the source of …o and protect other contacts

…e suggestion for a modified form of notification, …medical practitioners find it helpful, and the …tools service useful for better control of this …If some provision were made on the all purpose …"intimation as well as certification? A few …I put forward a modified notification form [1]

*FIRST SCHEDULE*

| | |
|---|---|
| …orm of certificate | Alternatively form of intimation. |
| …edical Officer of Health | To the Area Tuberculosis Physician |
| …ertify and declare that | Dr |
| | I have examined |
| | of |
| …from tuberculosis(†) | and suspect the patient may be suffering from respiratory/non respiratory tuberculosis |
| Sex | Age Sex |
| …or description | Occupation |
| | Medical condition |
| …part affected | I would like this patient to be specially examined for tuberculosis and a confidential report sent to me Attendance at the clinic can/cannot be arranged. |
| …ordinary residence if …from that at (†) above | |
| | Signed |
| | Address |
| | Date 19 |
| day of. 19 | If the suspicion of tuberculosis is confirmed a fee will be paid |

…address of place where person is living at the time
…for the purpose of the Tuberculosis Regulations
…any significant departure from normal health due
…activity of a tuberculous lesion

…Shelton,

G LISSANT COX

…Professor Illingworth and his colleagues have …further evidence of the desirability of …the use of B C G vaccination to newborn …thereby protecting them during their first five …before they face such hazards as the infant welfare clinic! All such additional evidence makes us regret that official blessing was not given to its general use in this age group when it was extended to school leavers

May I comment on one point? They frequently found that children had become infected because the adult contact was sputum negative at the time of examination and so the child was not vaccinated Surely this is not the usual practice? In this clinic and in many others all children with a tuberculous family history are vaccinated and indeed our use of the word 'family" is very elastic we include friends and neighbours It is much simpler to vaccinate when the adult case is *quiescent*, as segregation is then unnecessary We have frequent proof that this policy is justified, so often when the children return for their annual Mantoux test we are told that the contact has had a relapse and is in bed at home or back in a sanatorium

The B C G Clinic,
The Hospital for Sick Children
London W C 1

MARCIA HALL.

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[1] *Med Offr* 1951 89 101

## ISONIAZID

SIR—During the past few months we have seen a few tuberculous patients who, while undergoing drug treatment progressed to cavitation from a soft fairly well circumscribed pulmonary lesion they were undergoing a six week course of streptomycin and isoniazid followed by six weeks of p aminosalicylic acid (P A S) and isoniazid

As there appears to be some evidence that isoniazid may be responsible for this 'softening process, would it not be safer to refrain from using isoniazid in this type of case, until either the patient does not tolerate P A S or the tubercle bacilli become resistant to it?

Holywell Hospital
Watford.

N D J da S WIJESEKERA

## 'EPIDEMIC VERTIGO"

SIR,—Dr Leishman's excellent observations in your issue of Jan 29 are most timely It is of interest to record the experience of my partners and myself during the last six weeks of 1954

Dr Leishman's description of his cases is in fact identical with our observations here with the one exception that there was always a short but definite pyrexial period which lasted from half a day to four days. The patients were apparently all in good health before the sudden onset The first symptom was vertigo or severe giddiness and dizziness, followed by vomiting without an abdominal cause or just nausea aggravated by movement of the head or even bed

In the 4 cases which I saw myself diplopia was present only once A complaint of tinnitus was never elicited There was no evidence of ear disease in any of these cases. 2 patients have been slow to recover fully but the other 2 lost all their signs and symptoms within three weeks Nystagmus was present in 3 cases. There were no other signs or symptoms to point to any other disease These 4 cases were therefore certified on the National Insurance certificates as acute labyrinthitis" (I was not aware of the epidemic vertigo classification)

We did not carry out the full investigations described by Dr Leishman, as we were convinced that these attacks of vertigo were in fact associated with the fairly widespread influenza epidemic during the same weeks Certainly in 2 cases there was no doubt for a different member of each of the 2 families was just recovering from influenza (of a fairly definite pattern and some severity) and in 1 of these cases another member of the family developed influenza five days later with a sudden onset of vertigo The incubation period in these two families seemed to be five to seven days, which corresponds to the incubation period experienced with the then prevalent influenza B epidemic

My partners and I found in this influenza epidemic that the most frequent symptoms were pyrexia, bone or joint and back pain abdominal pains and vomiting dizziness and vertigo nose bleeding mild conjunctivitis, and upper respiratory infection; and occasionally meningism and photophobia. The tonsils were often mildly injected.

Nose bleeds became embarrassingly frequent and the many alarming messages taxed our telephone and reception organisation to the full At least 3 patients required treatment by cautery The influenza was commonly associated with acute vomiting (with or without abdominal symptoms), and this made many return visits and surgical consultations necessary

We estimated that vertigo was present in 1 out of every 7 adults, and in 1 out of every 10 children It often lasted for only part of a day, but sometimes for as long as a week In at least 2 adults nystagmus was observed with the usual influenza symptoms, but disappeared after two and three days, neither case showed evidence of any intracranial lesion.

The 4 patients with pure vertigo, or acute labyrinthitis, were treated with rest in bed, and a fluid diet (because of vomiting), 'Avomine' (promethazine 8 chlorotheophyllinate) was given in 2 cases No other drug was used

The infectivity may be largely explained by the geography of this area there are only a few transport services (used by practically everybody), few shops, and a high density of population

No case of encephalitis occurred during the period, or has appeared since, in our practice The 1 case of influenzal meningitis was in a child, who has recovered

The total number of influenza cases which the 6 of us treated during these six weeks we estimate at 980, out of a population at risk of approximately 16,000

Our experience suggests that "epidemic vertigo" may be a single manifestation of an influenzal virus infection One wonders whether the vomiting seen in this influenza epidemic was in fact cerebral in type, but masked by other signs and symptoms of influenza

A fuller report of this influenza epidemic and of its implications (especially in connection with the condition called epidemic vomiting) is being prepared by us for the research committee of the College of General Practitioners

Edinburgh E V KUENSSBERG

SIR,—Dr Leishman's report of a small series of cases of this peculiar syndrome in which he was able to demonstrate oculomotor complications is of particular interest to me In the cases which I reported [1] there were no such complications, but it might be of value to him to hear of a case which I have seen, but have not dared to publish in view of the inability to establish a definite diagnosis

A healthy man, aged 40, suddenly developed vertigo and diplopia when walking home from a football match This was followed by nausea and vomiting

On examination there was a left-sided third nerve lesion as evidenced by internal strabismus and some ptosis There was irregular rotatory nystagmus to the left and partial lower left facial weakness, and the left hemipalate moved less well than the right There were no other abnormalities in the central nervous system The blood pressure was 140/80 mm Hg, the heart was normal in size and shape and regular in rhythm There were no abnormalities in the respiratory system or the alimentary system, and the patient was apyrexial

When the patient was removed to hospital long standing bilateral catarrhal deafness was found. X ray examination of the chest and skull was negative The blood picture was normal, and lumbar puncture yielded clear colourless cerebrospinal fluid under normal pressure, with free dynamics, laboratory examination of the cerebrospinal fluid did not reveal any abnormality A full examination of the optic discs, fundi, and visual fields was carried out (but in the case of the visual fields this was not done until some time after the onset of the disease), and once again no abnormality was found

Both the symptoms and the signs were transient, and the patient made a complete and uninterrupted recovery Now, about three years later, the patient is leading a very active and strenuous life without any recurrence of trouble

I admit that it is difficult, if not impossible, to exclude a small localised thrombotic lesion It was also postulated that anterior poliomyelitis could not be ruled out All I claim is that the sudden onset and the similarity of the presenting symptoms, in an otherwise perfectly fit man, bear a striking resemblance to the cases of "acute labyrinthitis" which I saw—and still see more sp modically—in this practice

Whatever the ætiology—and the evidence suggest virus infection—does it not seem possible that a syndro which includes oculomotor complications might demonstrate, in some cases, involvement of other cra nerves ? The present state of our knowledge supp the wisdom of Dr Leishman's opinion that "epide vertigo" is a preferable title to "acute labyrinthiti

Corsham, Wilts W L BURROWE

## STERILISATION OF SYRINGES

SIR,—In your annotation of Jan 22 you state autoclaving is an unsatisfactory method of sterilis because the syringes have first to be taken apart

If 'Vim' syringes are used (and in my opinion t are the best syringes available in this country at present time) they can be assembled, placed in tubes, and routinely subjected to autoclaving temperature of 120°C (15–20 lb pressure) for 20 min and this I consider a most satisfactory metho sterilisation

Hull W N ROLLAS

## TREATMENT OF ACUTELY PERFORATE PEPTIC ULCERS

SIR,—One of the most interesting observatio Mr Moore's article (Jan 22) is that of the fail radio opaque material to traverse the pylorus in cases of duodenal perforation This is the co type of perforation, and those who favour the adv of "conservative" or "aspiration" treatment may have to consider the efficacy of suction in these Elsewhere [1] I have suggested that by aspiration on only withdraw some of the gastric contents, and in of duodenal perforation it may not be possible to away the duodenal and small intestinal fluid which up from paralysed loops of bowel In my opinio much reliance is placed on aspiration by the adv of nonoperative treatment, and Mr Moore's radiol findings support the conception that pyloric spa œdema is present to a degree which must diminis value of aspiration

Department of Surgery,
University of Liverpool J A SHEPHE

## CEREBROSPINAL FLUID IN CARCINOMATOSIS OF THE MENINGES

SIR,—These changes are as yet inadequately apprec and Dr Murphy (Jan 29) again draws attention syndrome He mentions the difficulty in distingu the condition from tuberculous meningitis The simi to the C S F changes in subacute meningitis are ob and yeast infections must also be considered neoplastic process may result from metastasis ( from a bronchial neoplasm) or may represent a gliom of endogenous origin Brain tumour may be simu as in the case recorded by Valaitis [2], electroence graphic abnormalities suggestive of a deep cerebral were present

A further interesting feature of the case was the f in the first C.S.F examination of only 8 cells per with a pressure of 215 mm of water and a protein c of 190 mg per 100 ml This low cell count wa constant, and one week before the patient's death the was 4905 cells per c.mm. In the subsequent discu H H. Merritt points out that the combination of inc pressure, pleocytosis, and decreased glucose content C.S F may be encountered in sarcoidosis, he quotes Pe who described this association with sarcoidosis in 1951

Victoria Hospital, Burnley J SHAF

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[1] *Brit med J* 1952 ii 1182

[1] *Brit med J* 1950, i 438 *Lancet*, 1951, i, 176
[2] Valaitis, J *J Amer med Ass* 1954, 156 719
[3] Pennell W H *Arch Neurol Psychiat* 1951, 66 72

## EART FAILURE DURING TREATMENT WITH PENTAPYRROLIDINIUM

ir,—The experience of Dr Ronnov-Jessen (Jan 15), the treatment of hypertension with pentapyrroli em in some cases precipitates congestive cardiac r has been mine also It is my unconfirmed impres that the patients thus affected are those whose renal ion is already considerably impaired

one such case (of nephrogenic malignant hypertension) t I have in mind, the patient has also suffered for over n years from bronchial asthma, and treatment with ion-blocking drugs (at first hexamethonium bromide by tion, and more recently oral pentapyrrolidinium) in ion to causing massive leg œdema, controllable with tics, has also worsened his asthma.

ilst the ganglion blocking drugs act upon both sympa and parasympathetic ganglia, their beneficial effect in tension is due in particular to their reduction of *sympa* tone arteriolar constriction. Under such circumstances perhaps not to be wondered at that an asthmatic hyper should find his *asthma worsened inversely* with the ovement in his blood pressure when treated with lion blocking drugs.

astle upon Tyne LESLIE J LEVENE.

## TIFICIAL HIBERNATION IN POLIOMYELITIS

ir,—We read with interest the observations of ehme (Jan. 15) and Dr Rollason (Jan 20) We recently tried artificial hibernation with 'Hyder ' in a severe case of poliomyelitis with hyperpyrexia

patient was tracheotomised and confined to a positive re respirator (Lundia) When the patient was hyper ic it was hardly possible to *maintain* the *respiratory* with the respirator Under hibernation however, the en needs were much reduced and the arterial $pO_2$ rose rmal value Body temperature was lowered to 33°C patient was put into a twilight sleep from which however s possible to arouse him *whenever desirable* There were convenient side-effects in the water and electrolyte lance, kidney function or circulatory system

think it justifiable to use artificial hibernation in treatment of poliomyelitis in the acute stage.

nna Sjukhuset
lmö, Sweden.

KNUT HAEGER
GUNNAR MIÖRNER
HANS RYD

## DRENALECTOMY FOR HYPERTENSION

r,—Mr Hanley (Jan 22) *advocates* the use of total al adrenalectomy for malignant hypertension and gests that most clinicians would agree that once dema has developed the expectation of life can be ured in months not years so the patient has to lose by undergoing this operation

should be remembered that series of cases of all forms of subjected to lumbodorsal sympathectomy have lished[1 2] showing in large numbers of malignant cases the five-year survival rate is 50% or above This is in es with definite papillœdema, which is the sole criterion ignancy adopted by most clinicians Mr Hanley does e whether this sign was present or not in his series.[3] without papillœdema but with advanced eye-ground es, the survival rate is 80% or better after five years. sympathectomy has a much lower mortality nd does not condemn the patient to a life-long dependence ication therapy which frequently needs constant ment.

It would be unwise to advocate complete adrenalec in all cases of malignant hypertension until long sults are available The present evidence is that adrenalectomy does not give as good a prospect ation of life as lumbodorsal *sympathectomy* with removal of both cœliac ganglia

W 1 FRANK D ABREU

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[1] thwick, R. H J *Amer med Ass.* 1951 147 1611
[2] Evans, F *Lancet*, 1953 i 1161
[3] Hanley H. G *Proc R. Soc. Med* 1951 47 1013

# Public Health

## Health in 1951

IN his report[1] on national well being in 1951 the Registrar-General reverts to his pre-war practice of reviewing civil and medical statistics in one volume, thereby greatly enhancing the value and interest of the survey

By 1951 we had apparently achieved stability the birth rate had settled at a level above the nadir of the economic depression of the nineteen thirties. 1060 males were born to every 1000 females. With the decline in *infant mortality, and the resultant increase* in the number of males surviving to maturity, the proportion of men to women has risen steadily since 1921 A simultaneous increase in the marriage-rate resulted in 1951, in the proportion of married women in the *total female population aged 15–19 rising to* 83% above the 1938 level Not only are women now more likely to marry, but they tend to marry younger—with all that this implies for fertility

Mortality rates in 1951 were dominated by the influenza epidemic, which was worst in Northern England As the 647 000 extra unseasonal disability claims made on the Ministry of National Insurance testify the sickness was widespread; but deaths were only 8% above the 1950 level Nevertheless the seriousness of the epidemic should not be under-estimated Liverpool had its highest weekly death roll since the cholera epidemic of 1849 there was too a check in the steady fall in mortality which has been going on since the end of the war (The male comparative mortality index was 8% below the 1938 level compared with 15% below in 1950) Infant mortality, at 30 deaths per 1000 live births, was the same as in 1950 and immaturity again bulked large as a cause of death. The continuing gradients between different parts of the country, legitimate and illegitimate births, and different social classes show that there is still room here *for improvement*.

In 1951 the notification rates for dysentery, whooping cough, and measles were exceptionally high. Poliomyelitis, on the other hand was *uncommon*, and diphtheria continued to decline As in 1950, food poisoning was (for no very apparent reason) notified most often in country districts or in larger cities. Tuberculosis remained an epidemiological enigma. Except for people over 65 death rates from tuberculosis fell precipitously from 1918 (although the influenza epidemic checked this trend, particularly in the North-West region) yet notification rates, particularly in the sensitive 15–25 age-group, were higher in 1951 than before the war Some at least of this *increase* is *accounted* for by the large number of minimal lesions discovered by mass miniature radiography, as well as by more intensive case-finding but there is still disquieting *evidence of* excessive mortality and morbidity rates in the Tyneside and Merseyside conurbations *and in* the industrial cities of the West Midlands Wales too, shares this excess in both respiratory and non respiratory forms of the disease

Similar geographical patterns are seen in the distribu*tion of mortality from* non infectious disease Bronchitis and cancer of the lung, for example, are especially common in Merseyside and the West Midlands, while coronary thrombosis and hyper*tension* are, in general, commoner causes of death in town than in country Age-trends in *some of* the non infectious diseases are also significant. Coronary disease and cancer of the lung continue their dramatic rise. Prostatic cancer has lately declined among men below 61 but for cancer of other sites, death rates by age-groups are, on the whole remarkably *and* depressingly stable. There are two important exceptions: among women 35 and 44, uterine-cancer death rates have ceased decline, and mortality from cancer of the br increased Among children the death rate (which is now included in the cancer shows a rise which, since it probably diagnosis, may be more apparent than real On one point there can be no doubt the rising death-rate from accidental swallowing of drugs among children under 5 points to an obvious cause and a ready cure

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[1] The Registrar-General's Statistical Review for the Year 1951 Text Volume Pp 312 10s

### Smallpox in Europe

The French government reported on Feb 9 that cases of smallpox in the Vannes area of the Morbihan department totalled 67, 15 patients have died 52 of the cases have been in hospital patients, so the fatality rate has been relatively high The last cases were notified on Jan 31 Over 2 million persons have been vaccinated in Morbihan and the four adjacent departments No additional cases have been reported from the Vosges department, where a vaccination campaign has been started In addition, instructions have been given to all departments to encourage the population to be vaccinated

The Belgian government reported on Feb 10 that 2 confirmed cases of smallpox had been notified at Spa—on Jan 31 and Feb 2 Extensive precautions have been taken by the health authorities

## Parliament

### Plans for New Hospitals

In the House of Commons on Feb 9 Mr Iain Macleod, the Minister of Health, made a statement about the Government's plans for increasing the rate of hospital building in England and Wales

It was proposed, he said, to expand the building programme both by starting new major building projects, including new hospitals, and by a special allocation of *money for replacement and redeployment of plant*

It was not thought that any significant increase in capital expenditure on major schemes could be achieved *in the 1955–56 programme, which remained unaltered* It was proposed in 1956–57 and 1957–58 to start new projects to the value of £7$^1/_2$ million and £10 million respectively For replacement and redeployment of plant £2 million would be available in the first of these years and £4 million in the second Apart from these amounts, there would be £9 million available in 1956–57 and £10 million in 1957–58 for capital expenditure on other works It was difficult to be precise about the total annual expenditure in these two years, but it was expected to be about £13 million and £18 million respectively These figures covered only work financed from Exchequer funds He hoped that a fair amount of hospital building work would also be financed from other sources during this period

Final details could not be given at the moment, but the boards concerned had already been asked to complete the planning of a first batch of major projects, to a total value of some £7 million, and these would almost certainly be among those started They included new general hospitals, or the first stages thereof, for Welwyn, West Cumberland, West Cornwall, Harlow, and Swindon, the development of the Glangwili Hospital, Carmarthen, a new mental hospital near Wolverhampton, major extensions at mental-deficiency hospitals in the Newcastle, Sheffield, and Liverpool regions, and in Wales, new outpatient departments at the Royal Victoria Infirmary, Newcastle, the Leeds General Infirmary, Lewisham Hospital, and North Middlesex Hospital, a new block at St *James's Hospital*, Balham, and major extensions to the Peterborough Memorial Hospital

Considerable expenditure was likely to be needed to repair structural defects at the Manchester Royal Infirmary There would also be many other projects which would need to be considered for inclusion, in the light of the further discussions to be held with hospital boards and the progress made with their preparation, and no firm list of these could be given at this stage *Examples of the type of project he had in mind to start* within the next few years were the new Cardiff teaching hospital, the rebuilding of Charing Cross Hospital at Harrow, a new ward block at Guy's Hospital, new general hospitals at Slough, Boston in Lincolnshire, Coventry, and Sheffield, and new mental hospitals in Lancashire and Yorkshire *He could not at present say which of these* would be started in 1956–57 and 1957–58

Mr H. A Marquand asked what forms of hospital bui work would be financed from "other sources" and wh the projects which the Minister had mentioned in detail the priorities assigned to them had been worked out in sultation with the Central Health Services Council. Macleod said that his mention of work financed by sources than Exchequer funds referred to the possibility a wealthy hospital with endowments of its own might co bute towards the expenses of a scheme which could n met from Exchequer finances He had had no sp consultation with the Central Health Services Council.

In reply to further questions Mr Macleod said that programme was in addition to the normal capital alloca made to the hospital boards He was not unduly w about the staffing problem With all the difficulties, ther been a steady increase since 1948 in the numbers of and this was continuing It would be easier to attract to good new hospitals than to old ones The Cardiff tea hospital retained the first priority in England and Wal a completely new teaching hospital But the archite *competition had not yet taken place* It was propos build the new Charing Cross Hospital at the site al obtained at Northwick Park, Harrow Whether or *would get into the 1957–58* programme depended on things, but it stood a good chance

Commander T D Galbraith, joint parliame under secretary of State for Scotland, announc similar programme for Scotland The total provisio hospital building, he said, would be increased £1 9 million this year and next, to £2 2 million in 19 and to £2 5 million in 1957–58 £50,000 in 1956–5 £150,000 *in 1957–58 would be used to supplemen* present special programme of plant renewal, on altogether £800,000 would be spent in the three *1955–58 The balance would be used to increas* number of major building schemes undertaken, a expected that it would be possible to put in hand sc *to a total value of £3 million during these three ye*

In 1955–56 a start would be made on a new mat hospital at Bellshill, Lanarkshire, a new surgical at Kirkcaldy, and the reconstruction of a mental ho in Dundee. Details of the subsequent programm still to be settled in consultation with regional bo boards, but among the projects to be considered extensions to mental-deficiency institutions at Ban in the Glasgow area, a new treatment unit at Gl Western Infirmary, reconstruction of the Edin Royal Mental Hospital, and improvement of ho facilities in Shetland Detailed planning work also be put in hand for other schemes to start in 19 and succeeding years, including the provision of teaching hospital in Dundee

### Capital Punishment

In 1948 the House of Commons, on a free vote, a clause to the Criminal Justice Bill to suspen death penalty for five years The new clause was th out by the House of Lords and the Government day accepted this rejection A few months later *appointed a Royal Commission to discuss wheth* death penalty should be "limited or modified" their terms of reference the commission were prec *from considering whether capital punishment shou* retained or abolished The commission report 1953 [1] On Feb 11, some sixteen months later, the *of Commons considered the commission's* finding the first time Inevitably the discussion covered of the same ground as in 1948, the same amend *to suspend the death penalty, was even introd* There were two differences The amendment was and this time no-one suggested that a mistaken exe *was a near impossibility in this country*

#### THE COMMISSION'S REPORT

Major Gwilym Lloyd George, the Home Secr said that three recommendations of the commission of outstanding importance The first was that statutory age-limit below which sentence of death not be passed should be raised from 18 to 21 second was that the jury should be given discreti whether there were extenuating circumstances to ubstituting a sentence of life imprisonment for eath sentence The third was that the test of al responsibility laid down in England by the ughten rules should be abrogated and that the jury be left to determine unfettered by any formula, er at the time of the act the accused was suffering a disease of the mind, or was mentally deficient h a degree that he ought not to be held responsible

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[1] See *Lancet* 1953, ii, 713

Government shared the natural desire to spare a life wherever possible, but they felt that it would ngerous and inopportune to raise the age limit at e when crimes of violence by people between 17 1 were so prevalent. In 1938 the number of people en 17 and 21 found guilty of such offences was in 1948 405; in 1951 492; and in 1953, 603

commission s proposal to vest discretion with the , which was not a positive recommendation had been ised by the Lord Chief Justice and three former Secretaries during a debate in the House of s, and the commission itself had recognised its dis ntages. The Government felt little doubt that it unworkable and ought to be rejected

majority of the commission held that the on of criminal responsibility contained in the ughten rules was defective in the light of rn medical knowledge and that the best course d be not to frame a more up-to-date criterion, to leave the jury to decide whether at the time of the accused was suffering from disease of the mind or al deficiency to such a degree that he ought not to be responsible Three members of the commission that some criterion was needed In their view a h limited the arbitrary element and promoted rmity To have no formula would leave the ion, on which a man s life might often depend to the tain variations of ethical standards and emotional ion which might influence the minds of the jury

Government shared the view of the minority that and some formula was essential They recognised the McNaughten rules were open to criticism but also noted that the commission admitted that the ical defects of the rules led to little hardship or e in practice. The Government were impressed difficulty of framing a satisfactory amendment rules, and by the wide differences of opinion on among doctors, lawyers, and the general public light of these considerations the Government felt o advantage would be gained by disturbing the t position and that it was better to leave matters y are

commission had recommended that the mental of every prisoner charged with murder should be ed by two doctors, of whom one at least should outside psychiatrist and the other usually an ienced member of the prison service This recom ation had been already accepted and it was now ce to consult an outside *psychiatrist where* as reason to believe that any difficulty was likely about the mental state of the accused These, were the Government s provisional conclusions commission s principal proposals

### SUSPENSION ?

ating the amendment for the suspension of the penalty, which he understood was to be moved that if a satisfactory alternative could be found ll welcome abolition But until such an alterna ted the death penalty must remain The Govern ere opposed to its abolition for three reasons. they were not disposed to reject the of many experienced people that it was a effective deterrent to professional criminals there had been a continued increase in sexual and of crimes of violence against the person Government held it was not the moment to the sanction of the death penalty

ly the Government were not convinced that tion of some murderers for long periods possibly whether in ordinary prisons or in special institu r mentally abnormal prisoners, would not give ore serious difficulty than the commission Some of the most heinous murderers were mentally abnormal, and it might be that they could be properly detained in special institutions for long periods but many, such as poisoners were mentally normal and would have to be detained in prison for a long time, even for life It was unlikely that such men would be suitable for detention in an 'open' prison, and their detention for more than twenty years in the conditions of a closed prison would be likely to lead to serious deterioration, as well as causing grave problems of security

Thirdly, the Government believed it would be wrong to abolish the death penalty without evidence of overwhelming public sentiment in favour of the change. They had no evidence that public opinion was in favour of abolition Indeed they believed that the contrary was true

The suggestion to suspend the death penalty for five years was, in the Government s view, misconceived The period would be too short to enable Parliament to form a reliable judgment of the effects of the change. If the experiment proved unsatisfactory, a difficult and confused situation might arise Such a 'trial period', would be likely to prejudice the whole future consideration of the question and, in fact meant the permanent abolition of capital punishment under the guise of what purported to be an experiment. The Government had no doubt that if a change in the law were to be made, the right course would be to face the issue squarely and to abolish the death penalty outright.

Mr **Chuter Ede** regretted that the Government proposed to leave the McNaughten rules unreformed A great deal more was now known about how the human mind worked, and occasionally failed to work, than when the rules were framed He thought that it would be an advantage to jurors if they had something more in accordance with modern modes of thought to help them in making their decisions. He agreed that prolonged detention in the present prisons for the most violent type of prisoner could not be readily tolerated But his experience was that the reprieved murderer was among the mildest mannered and best behaved inhabitants of our prisons. He did not think that the case for or against the death penalty as a deterrent was proved. He doubted too, whether, at the moment, public opinion was in favour of this change but he also doubted whether at any time during the last hundred years a plebiscite would have carried any of the great penal reforms that had been made There were occasions when the House had to say a thing was right even if the public at the moment were not of that opinion

Mr **Sydney Silverman**, moving the amendment to suspend the death penalty, urged that five years would give the Home Secretary an experimental period and a chance to educate the public He pointed out that the other problems including insanity and degrees of moral culpability vanished if the death sentence went.

### THE REST OF US

Mr **Christopher Hollis** in seconding the amendment, said that throughout the nation today there was a morbid obsession with murder In the Scandinavian countries and Holland the atmosphere was different, He had no doubt that a large part of this morbid interest came from the drama of a man on trial for his life. To be effective, deterrents must be as humdrum and undramatic as possible Mr **Basil Nield** on the other hand after many years experience in the courts held that the final ultimate, and most cogent of all deterrents is the contemplation of the death penalty' The McNaughten rules, he agreed should be retained but he suggested that they should be extended to include defect of will as well as defect of reason

Sir **Frank Soskich** did not believe that the fact that the death penalty might be a deterrent was sufficient to justify its retention Nobody would suggest that we should reintroduce physical torture, yet that was the most effective of all deterrents Against its advantages as a deterrent we must set the harm the death penalty did to society All the lurid and graphic details were drunk in by millions of people In the long run he believed it was bound to blunt the kindliness on which our civilisation rests.

### THE MCNAUGHTEN RULES

Dr **REGINALD BENNETT** thought that the McNaughten rules were useful, but had shortcomings which related not only to borderline cases Fortunately juries were not bound by the rigid doctrine of the rules As the Lord Chief Justice had pointed out, a jury could always be trusted to do justice where it might be impossible to bring a case strictly within the rules It must be faced that the rules were dangerous and misleading and only approximately did the job for which they were intended But nobody had found a substitute formula, and the commission's report had shown, in his view, that we could not do without a formula He agreed that diseases of the mind should not only refer to defects of reason , the term should be broadened to cover defects of will Most mental diseases, as they were known nowadays, were regarded as defects of the emotions, and in these diseases he thought it was true to say that the emotions governed the will The intention or idea of the principle of irresistible impulse was a good one, but it would entangle a jury in a welter of hypothetical motivations It was too subjective a test even in the modified form which the commission recommended Juries were not qualified to split hairs on psychiatric issues, but, as he saw it, they were qualified to judge sanity and recognise conduct within normal limits He suggested as a modification of the rules, in place of that suggested by the commission, that, if the answers to the existing questions—whether the man knew the nature and quality of his act, and whether he knew it was wrong—was " Yes " it would be possible for the jury to ask the further question " Were the actions consistent with sanity ? " If the answer was " No," the jury could then find the prisoner guilty on the facts of the actions with which he is charged, but " we do not consider his actions to be entirely consistent with those of a sane man, and, therefore, recommend him to mercy "

Sir **REGINALD MANNINGHAM-BULLER**, the Attorney-General, felt that the balance of the opinion of the House seemed to be that a formula was useful to a jury and that it would be difficult to find one which improved on the McNaughten rules Turning to the amendment he reiterated the Government's view that with the rising figures for crimes of violence we should not risk at this time abolishing or suspending the death penalty.

The amendment was rejected by 245 votes to 214

## Horror Comics

In the House of Commons on Feb 10, Major **GWILYM LLOYD GEORGE** presented the Children and Young Persons (Harmful Publications) Bill, which was given a formal first reading The Bill proposes to make it an offence to import, print, publish, or sell pictorial publications harmful to children and young persons The Bill applies to stories told wholly or mainly in pictures portraying the commission of crimes, acts of violence or cruelty, or incidents of a repulsive or horrible nature in such a way as to corrupt a child or young person

## QUESTION TIME

### N H S Prescriptions

Replying to a question Mr **IAIN MACLEOD** gave the following figures for prescriptions issued under the N H S in the month of November in 1953 and 1954

| *Month* | *No of prescriptions* | *Average cost per prescription (d )* | *Total cost (£)* |
|---|---|---|---|
| November, 1953 | 18 512 492 | 47 47 | 3 661 862 |
| November 1954 | 19,785,862 | 51 14 | 4 215,069 |

### Shortage of Hospital Pharmacists

Replying to a question Mr **MACLEOD** said that the shortage of pharmacists was not peculiar to hospitals He was considering what could be done to solve the problem in hospitals, in the light of information he had recently obtained from them A salary claim for hospital pharmacists was at present under consideration by the appropriate Whitley Council

### Textbook on Aviation Medicine

Dr A D D **BROUGHTON** asked the under secretary of State for Air what standard textbook on aviation medicine had been adopted for the use of medical officers of the Royal Air Force —Mr G R **WARD** replied Armstrong s *Principles and Practice of Aviation Medicine* Dr **BROUGHTON** Is the Minister satisfied that that book is up to date in its contents , and, as there is a very good book written by a British au which is recommended for use in the air forces of Austr Canada, New Zealand, India, and Pakistan, why is this b not recommended for use in the Royal Air Force ? I Dr Bergin's *Aviation Medicine* —Mr **WARD** Mr Armst is an American author whose book was published in country in 1952 by Baillière, Tindall, & Cox, and it, I think, generally accepted to be the best reference wor the subject so far produced. Of course, Dr Bergin's boo also available in Command libraries It was on the ad of the Institute of Aviation Medicine that we adopted Armstrong's book as our textbook

### Medical Standard of National Service Recruit

Replying to a question Mr **HAROLD WATKINSON**, pa mentary secretary to the Ministry of Labour and Nat Service, said that the number of men classified as grade III who were conscripted in 1954, 1953, and 1952, 8050, 7690, and 8189

### Tuberculosis Eradication Plan

Replying to a question Mr **HEATHCOAT AMORY**, Mi of Agriculture, said that preliminary discussions had rec taken place about the next areas to be dealt with unde tuberculosis area eradication plan The proposal as re the five counties—Berkshire, Hampshire, Surrey, Sussex, and the Isle of Wight—was to provide free tube tests from March 1, 1955, in the expectation that these might be declared eradication areas two years later subsequently attested areas

### Medical Grading of National Service Recruit

Replying to a question, Mr **HAROLD WATKINSON**, mentary secretary to the Ministry of Labour, said the number of men called up for military service in 195 147,975 In addition 52,840 men in the national servic of call up joined the Forces on regular engagements the year The number rejected on medical grounds was 51,000

### School Dentists in Scotland

Replying to a question, Commander **GALBRAITH** that at Dec 31, 1954, the equivalent of 172 whole time officers were employed in the school dental service in Sco

### Free Moneys for Hospital Capital Works

Mr **ARTHUR BLENKINSOP** asked the Minister of whether he was aware that hospital management comm were being increasingly forced to use free moneys for capital work, such as sanitary annexes and heating install because of the inadequacy of capital allocations , and to extent he had approved this practice —Mr **MACLEOD** re I see no objection of principle to the use of non Exc funds for such work.

### Hospital Visiting-hours

Replying to a question, Mr **MACLEOD** said that his information was that of 1362 hospitals admitting ch 852 ($62^1/_2$%) allowed daily visiting, compared with les 25% in 1952 Many others allowed visiting on at least days a week He was not dissatisfied with the progress made

### Clinical Experiments on Child Patients

Mr S T **SWINGLER** asked the Minister of Health w he would ensure that, before further clinical experime children were undertaken, the nature of such exper was reported to his department, so that his medica could ensure that there were adequate safeguards a harmful effects , and whether he would issue a direct hospital management committees on the ethical pri which should govern the conduct of clinical exper with particular reference to the importance of secur consent of the patient —Mr **MACLEOD** replied On clinician in charge of each patient can say what safegua needed I do not think, therefore, that directives or d controls would help in this matter

### Fluoridation of Water-supplies

Replying to a question, Mr **MACLEOD** said that a pilot of urinary excretion of fluoride in children was m London during 1953 and 1954, and 36 children up to the twelve were under examination It confirmed the obtained in the United States and New Zealand and m clear that more extensive studies were unnecessary cumstances he did not propose to publish the results as not envisaged that such examinations should be made ally after fluoridation had started. The mission which ied fluoridation in North America only raised the question nary examinations in connection with the preliminary ment of the right amount to be added

### aynaud's Phenomenon and Industrial Injuries

plying to a question Mr OSBERT PEAKE Minister of ns and National Insurance said that he had decided pt the advice of the Industrial Injuries Advisory Council Raynaud's phenomenon should not be prescribed under dustrial Injuries Act 1946

## Obituary

### FELIX BOLTON CARTER

M.S. M D Lond., F R.C.S.

Bolton Carter honorary consulting surgeon to the ster Royal Infirmary, died on Feb 5 at the age of 81 qualified from University College Hospital in 1895 took his M.D two years later After holding house ointments at U.C.H and at the Royal Infirmary ax, he took the F.R.C.S in 1899, the B.S with first honours in 1901, and the M.S the following year while he had settled in Leicester where his first ointment at the Royal Infirmary was that of house-on to C J Bond, who had won a national reputation ly as a surgeon but also in particular, for his ches in genetics. When Bond retired in 1912, Carter succeeded to his private and hospital ice. Apart from his service with the R A M C he nued his work at Leicester until he retired in 1933 colleague writes: 'Bolton Carter was the first ified surgeon appointed to the Leicester Royal mary as such. All earlier surgeons had also been in al practice At the time of his appointment there few special departments, and he operated with the t skill not only in ordinary general surgery but ecology and orthopædics, and he also practised radio py He was undoubtedly a first-class surgeon Out his profession he had many other interests. He d association football for the old Fosse Football which has now become the Leicester City Club as a keen golfer and was captain and president of estershire Golf Club; he also played an excellent of bridge. A brilliant surgeon and a kindly per- ty he will be missed by all the friends who knew for so many profitable years.

Bolton Carter leaves a widow three daughters, and Mr J P Bolton Carter who is an assistant surgeon I.H.

### JOHN BRUCE LOW

M.B Edin., D.P.H

Bruce Low a divisional medical officer of the n County Council, died at the age of 65 in West- Hospital on Jan 24, a week before he was due

father was Edward Bruce Low S.S.C. of Edinburgh, e was educated at Merchiston Castle School and versity of Edinburgh where he graduated in in 1913 At the outbreak of war the following joined the Red Cross and he was among the first to France Later he transferred to the R A.M C the war, on the advice of his uncle Dr Robert Low, he entered the public health service He staff of the L.C C in 1920 and he took the in 1921

the next twelve years he worked in the school service in London till, in 1934, he transferred work on the council's accelerated programme of clearance under the Housing Acts. When the second war brought rehousing to an abrupt stop he to the school medical service as medical officer of the north western division He handled the unusual work involved in the evacuation children from London and later in rebuilding on their return. A colleague writes: 'Bruce been brought up in the traditions of the founders service he devoted all his zeal and energies to the of the children of London and to the improvement of their lot, physical, mental, and psychological Careful, conscientious, and sound in judgment, he had also a sense of humour that endeared him to his colleagues To everyone whom he met child or adult, he was courteous, quiet, and sympathetic.'

Dr Bruce Low leaves a widow and a daughter

### LAWRENCE MICHAEL EKEN RICHARD HENSHAW

O.B.E, M.B Edin., D T.M & H, L.M

Dr Lawrence Henshaw a former senior medical officer in the Nigerian medical service, lost his life in an air crash near Calabar on Feb 5

He was born in 1898, the son of the political agent who accompanied Lord Trenchard on his Aro Bendo expedition He went to school at the Sacred Heart School Calabar, and at King's College Lagos A brief spell as a dispenser stood him in good stead when he went to Edinburgh University to study medicine He qualified in 1927, and before he returned to Nigeria in 1928 he took the further qualifications of L.M. and D T.M & H He entered the Nigerian medical service at once and became a medical officer in 1930 In 1948 he was promoted senior medical officer Soon afterwards he was appointed O B E In 1952 he retired from the government service and became doctor to the Palmol estate near Calabar his home town.

C W writes: 'As a colleague Henshaw was staunch, helpful and kind As a friend he could not be bettered, while his quiet joviality was a tonic in hospital, at meetings, or in the home His sterling worth and sound common sense were well recognised and he had lately been appointed to the governing body of the new University College at Ibadan He was returning home from a meeting of the council of the Nigerian College of Arts, Science and Technology, of which he was also a member, when he met his death. Nigeria and the Commonwealth have lost a fine citizen'

## Appointments

AYLWIN, J. A M.B. Leeds, F.R.C.S: asst surgeon, department of thoracic surgery, United Leeds Hospitals, and consultant thoracic surgeon to the Leeds R.H.B
BAMBER, WILLIAM M B Belf D.P.H: M O H co Antrim
CUTLER, G A. M B Sydney: registrar in obstetrics and gynæcology, Bath group of hospitals
DAVIES, MARGARET R M.B Wales, D.P.H asst. M.O Swansea
DONNISON AILEEN B M.B Camb: asst. M.O The Hospital for Sick Children Great Ormond Street, at Tadworth Court.
EDWARDS, H C C.B.E. M.S Lond F.R.C.S consultant surgeon, Royal Masonic Hospital, London
HONY DINAH J M.B. Lond. registrar in anæsthetics University College Hospital of the West Indies St Andrew Jamaica.
JOEL, MARY B F., M.B. Edin. senior school M.O., Blackpool.
LENNON T E M D Lpool M R C.O.G D OBST hon. consultant gynæcologist Providence Hospital St Helens Lancs
MCNAMARA, KATHLEEN M L.R.C.P.I anæsthetic registrar Peterborough Memorial Hospital and annexes
MARSHALL, ANNABELLA M B. Glasg senior M.O West Riding of Yorkshire
MURPHY JOHN, M B Glasg D P.M. psychiatrist (S.H.M.O) Stratheden Hospital, Fife
OCKENDEN, BARBARA G M.B. Lond asst morbid anatomist, The Hospital for Sick Children, Great Ormond Street, London.
PORTER, RUTH M B. Edin. D C.H medical registrar, University College Hospital of the West Indies St Andrew Jamaica.
RIBCHESTER MARIE JOYCE, L.R.C.P.E. asst. M O H. Blackpool.
SCANLON J. A. M.B Lond.: anæsthetic registrar West Suffolk General Hospital
SCHULBERG BERTRAM L.R.C.P.E. school M.O and asst M.O.H. Coventry
SHEARER, C W M.B. Edin. D.P H asst. county M O H Kesteven, and M.O H borough of Grantham and West Kesteven rural district.
THOMSON MARGARET H M.B. Aberd. asst M.O Swansea
WALL, A E. M B Manc. M.SC., F R.C.S. asst surgeon department of neurosurgery, United Leeds Hospitals and consultant neurosurgeon to the Leeds R.H.B.

**Liverpool Regional Hospital Board:**

DE BOER, C H., M.B. Camb. F R C.S M.R.C.O.G: part time consultant obstetrician and gynæcologist, Liverpool Maternity Hospital, the Women's Hospital, and Warrington General Hospital
GIBSON JANE I M.B Aberd. consultant pathologist Birkenhead and north Wirral groups.
MCGUIRK, B H M R.C.P F F A R C.S. D.A: part time consultant anæsthetist, Chester and Wirral areas

**Newcastle Regional Hospital Board:**

ARNOLD F L., M.A. M B Camb D O.M.S consultant ophthalmologist Newcastle H M C.
CRANMER, J G., M B. Glasg F.F.A R.C.S., D.A consultant anæsthetist Northallerton H.M C
PILNICK S T., M.D Warsaw asst psychiatrist (S.H.M.O) Winterton Hospital Sedgefield

# Notes and News

## BIRMINGHAM UNIVERSITY'S FINANCES

In response to an appeal by Birmingham University, £439,000 has so far been contributed, and in his annual report Dr R S Aitken, the vice chancellor, says that the spending of the *first £50,000 has been "a tonic to the whole* university"[1] Already, he says, the money subscribed is achieving the first objective—to sustain research and teaching at least at their 1952–53 level, despite rising prices and salaries, and there is every hope of "a little expansion and improvement of quality in those parts of the university most constricted"—which was the second object of the appeal The "already high proportion" of university income from Government grants is to be increased under the agreement to provide facilities to increase the number of students in the faculty of science in three years from roughly 1280 to 1680, this expansion will eventually add £200,000 to annual income and expenditure "In spite of the considerable measure of freedom accorded to us by the University Grants Committee, such grants must broadly be spent on objects that have the committee's prior approval As that proportion rises so it becomes more difficult to preserve in the policy making bodies of the University—the Senate and the Council—the enterprise and the liveliness that accompany *freedom, the readiness to see and seize good opportunities* as soon as they present themselves A rise in non Government income, parallel with that in Government income but free from the delicate strings which radiate from Whitehall, would be doubly welcome *The appeal has given us something* of that for a limited period" Dr Aitken remarks that three fifths of the university's expenditure is on salaries and wages, and he asks whether, since 80% of university income is from Government grants fixed at quinquennial periods, there could not be enough planning or elasticity to budget for probable salary changes at the same time Of differences between salaries in the different faculties, Dr Aitken says "The salary that will make a university career attractive to a good arts professor, will not so often beckon the good scientist away from industry or high level pure research, and the salary that will make the good scientist feel that the university is worthwhile is less than the top flight medical man can easily earn from the Health Service or in practice These are facts which have no bearing at all on the relative value as scholars of the arts professor, the scientist and the medical man If the university levels all salaries down it will fail to fill its clinical chairs and many of its science and engineering chairs with first-class professors If it levels them all up it will be liable to the accusation of extravagance To attempt either would be doctrinaire" A common sense course of keeping salaries within reasonable limits is, he says, the only one Maintaining the quality of academic staff is the first requirement

## HUNTERIAN FESTIVAL

The Hunterian Festival dinner last Monday at the Royal *College of Surgeons of England was attended by a large* gathering, which included two Commonwealth prime ministers—Mr S G Holland of New Zealand and Sir Godfrey Huggins, F R C S, of the Federation of Rhodesia and Nyasaland Lord Adrian, O M, P R S, who proposed The College, relished the choice of a physician for this task. Not that there was anything amiss with the college's health On every visit there was something new to admire, including the latest Bentleys outside and stately new halls within Surgeons, he reflected, were about the only ones who could carry on with a clear conscience, after all, the physicians and the obstetricians between them were making a world fit only for gerontologists and pædiatricians *Casting his mind back forty five years* to the time when the heart was reserved for the physicians and the brain for the intellect (the psycho analysts had since told us how little the intellect matters), Lord Adrian was struck by the subsequent advances in surgery This was still an art as well as a science, but such duality, he apparently thought, was unlikely to persist, for, moving in imagination forward over the years, he forecast that the college might have to organise a great *replacement service of organs* guaranteed in working order Perhaps, too, the surgeon might operate without approaching the patient, applying the artery forceps as soon as the spectrum of oxyhæmoglobin appeared on the screen He pictured patients coming off t conveyor belt without the duodenum or frontal lobes that h hitherto made their lives a burden Sir Harry Platt president, in reply, expressed pride in the college's Hunter tradition, which, he said, was a living force and not, as mi be thought, a mystique Hunter was an empiricist n splendid age of reason The President referred to the awak ing of the college in the 1920s, when it turned back to exp mental surgery More recent years had been marked by presidency of Lord Webb Johnson, which would be rega by later generations as "unique in the history of the colle It was Lord Webb-Johnson who planned for new laborato the new hall, and a residential college—a plan that took sh in reality through the gifts of Sir William Collins and l Nuffield Sir Cecil Wakeley's subsequent presidency had distinguished by the creation of an institute of basic scie and the launching of a department of pharmacology final phase of expansion the college was to have new muse lectures theatres, and laboratories, and a cancer rese department The aim was to make the college a great acad of surgical science Lord Woolton, replying to Prof Lam Rogers's toast to The Guests, modestly asserted tha owed this privilege to influence "Your president *I fed at the same educational trough*" Lord Wo observed that within the space of a few years Manch had provided the college with two presidents (Lord W Johnson is the other), and, to still any doubts, he dec *that Manchester had many promising young men* comin Mr Julian Taylor, toasting Sir Cecil Wakeley, the Hunt Orator, likened him felicitously to Dick Whittington, congratulated him particularly on his work for the coll *Annals* Sir Cecil, eye on clock, responded with comp brevity and was warmly applauded

## HUNTERIAN SOCIETY

At the annual dinner of this society in London on Ja the Lord Chancellor (Viscount Kilmuir) spoke of Hunt "an inspiring figure who still enthrals us down the arc the years" After recalling the redoubtable courage H displayed in turning from his house a party of guests his wife, without asking his permission, had invited to di he went on to draw a parallel between Hunter's ideals those of the Hunterian Society the finest of Hu attributes—"the unquiet mind, the restless energy, an powerful determination to see that something new something understood'—flourished no less strongly successors of 1955 To medicine in all its branches H had been an eternally helpful godfather, and Lord Ki felt that in honouring his immortal memory he was, in acknowledging personal admiration for the profession whole Responding to a toast by Dr Gordon Sears, the Mayor of London (Sir Seymour Howard) pointed out th own office entailed duties curiously similar to those doctor both were concerned with the harmonious co tion of all the organs, but for him the organs were th the body politic—a patient notoriously lacking in grati In his reply to the Guests, proposed by Sir Arthur P the President of the Royal Academy (Prof A. E Richar recalled that William Hunter (John's elder brother) the first professor of anatomy at the Academy Noting anatomy and architecture were in fact closely allied, he confident that the society would join with him in conde the growing threat to London's skyline For the City rebuilt "on resplendent lines" it was essential for buildings to be kept to a reasonable height He look the City fathers to defy those who "cast envious e on the north bank of the river between the Tower and minster If Wren's magnificent skyline was to be prese a total reorientation of the planners' ideas was needed

## WORLD HEALTH ORGANISATION

The Executive Board of W.H O concluded its meeti Geneva on Feb 4 with a recommendation to the World H Assembly to accept the director general's proposals fo Organisation's 1956 programme and a budget of $9,61 Under the 1956 programme over a hundred countries territories will be aided in developing their health ser Sanitation, control of disease, education of health and mother and child health will be given particular atte The board approved the second four year plan of the Orga tion for the period 1957–60, but decided to call the atte of the World Health Assembly to the disparity bet resources and demands by governments for help in streng ing their health services

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[1] *Birmingham Post*, Feb 10 1955

## CORTISONE AND CORTICOTROPHIN FOR ACUTE LEUKÆMIA

Ministry of Health has accepted a recommendation by Medical Research Council that acute leukæmia should be ed to the list of conditions for which supplies of cortisone corticotrophin additional to those for ordinary treatment be sent to hospitals receiving regular monthly issues of substances. Additional supplies are already being sent ree hospitals for the following conditions Addison's adrenal hyperplasia, adrenalectomy pituitary dys ion, disseminated lupus erythematosus polyarteritis osa, pemphigus, exfoliative dermatitis, hæmolytic anæmia and sarcoidosis.

## CONTROL OF LEPROSY

in 1917 Sir Leonard Rogers was able to show that hydnocarpate could clear up the lesions of leprosy treated within three years of the onset he recognised the old policy of compulsory segregation of these patients positively harmful because it led people to hide their until the disease was too far advanced for effective ment. In a recent review of progress[1] he recalls that y in the early 1920s he was denouncing compulsory ation as a dangerous and expensive failure Between and 75% of infections, he then pointed out were con ed in childhood or adolescence and the incubation period d three and a half years. 95% were derived from close t with mucocutaneous cases through discharge of leprosy from the nasal mucosa. In a series of 700 cases in which of infection was traced nearly 60% of the patients ved in the same house as some previous case On these he based his plan for controlling leprosy by isolating only lepromatous cases, who were only a fifth of the total Children in the incubation period could be left in their , with the proviso that all contacts must be examined by each year for a decade As an example of the of the plan Sir Leonard described its application in and of Nauru in the Pacific where in 1912, leprosy was ced in the wake of an influenza epidemic Thirteen later the incidence was 300 per 1000 Then the Rogers adopted, with the result that the number of cases had by two-thirds eight years later The same system had en successfully introduced in South Africa South East a, East African Territories, India and British Guiana i it had been found necessary to retain compulsory ation, because of the scattered distribution of the disease many small islands of the group The West Indies also ve unnecessarily clung to compulsory segregation, appointing results.

prophylaxis of child contacts, Sir Leonard admitted ed a problem, but promising results had been obtained C.G. vaccine

th the prospect of control has improved in so many during the last forty years, some 100 000 children infected every year in British and Indian territories n there is still every reason to continue to support of which Sir Leonard was the far-sighted founder y in the nineteenth century" he said in conclusion, t Britain provided £20 million sterling—now worth s as much—to abolish slavery from our dominions. prosy in the disfigurement and the life long crippling ch it produces is worse than slavery What we is a modern crusade to provide the means now le to save our Empire children from the most cruel that human flesh is heir to

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### sity of Cambridge

4 the following degrees were conferred

Pippard

Johansson, *J F Wood

By proxy

### sity of London

25 the following degrees were awarded:

Sackling.

Connell.

F Hunt, senior lecturer at Guy's Hospital Medical has been appointed to the readership in physiology

### University of Leeds

Sir Howard Florey F.R.S will give a talk and demonstration on Monday Feb 28 at 4 P.M in the General Infirmary, on cinematographic Illustration of Some of the Phenomena of Inflammation.

### University of Edinburgh

The Edinburgh branch of the Infantile Paralysis Fellowship has given the university 1000 guineas to found a Lawrence Poole memorial prize to be awarded for a practical or theoretical contribution to the rehabilitation of poliomyelitis patients.

### Royal College of Surgeons of England

At a meeting of the council on Feb 10, with Sir Harry Platt, the president in the chair honorary fellowships were awarded to Dr Loyal Davis (Chicago) Mr William Doolin (Dublin) Prof Robert Janes (Toronto) and Prof. Paul Santy (Lyons)

Mr C W Flemming (University College Hospital) was re-elected and Mr D Ioan-Jones (Cardiff) and Mr T G I. James (Central Middlesex) were elected to the court of examiners.

Prof A B MacGregor (Birmingham) was appointed Charles Tomes lecturer for 1955 and the Hancock prize was awarded to P S Boulter (Guy's) Dr N M Cass was appointed lecturer in physiology

A fellowship in the faculty of anæsthetists was granted to R. W Milner Diplomas of membership were granted to P R Holt and to those named in the report of the comitia of the Royal College of Physicians (Feb 5 p 313) Other diplomas were granted to those named in the report of the comitia and to the following

*D P H*—I H Seppelt.
*D.I H*—Z. Khan.

### State University of Iowa

Dr J Maclean Smith F.R.F.P S has been appointed assistant professor in the department of medicine where he is to organise a new division for research, teaching and consultation in infectious diseases.

### Industrial Injuries Advisory Council

*Sir Arnold Plant* Sir Ernest Cassel professor of commerce in the University of London at the School of Economics, has been appointed chairman of this council in succession to Sir Wilfrid Garrett

### Chesterfield Medal

The form of the Chesterfield medal examination has been changed. From this year the medal (with a prize of £25) will be awarded to the applicant submitting the best essay on a dermatological subject selected by himself. Further details can be had from the dean of the Institute of Dermatology Lisle Street, London W C.2

### Microcirculatory Conference

This conference which is sponsored by the American Association of Anatomists is to be held in Philadelphia on April 5 The main subject chosen for discussion is vascular pattern as related to function Further particulars may be had from Mr G P Fulton, PH D the chairman of the conference College of Liberal Arts, 725 Commonwealth Avenue Boston 15 Massachusetts.

### James Yearsley Lecture

The medical staff committee of the Metropolitan Ear Nose and Throat Hospital have established an annual lecture to commemorate Dr James Yearsley who founded the hospital in 1838 Mr Terence Cawthorne will give the first lecture on Friday March 4 at 5 30 P.M., at St Mary Abbots Hospital, Marloes Road London, W.8 Mr Cawthorne will speak on surgery of the ear in the prevention and treatment of intracranial complications of chronic suppurative otitis media.

### British Occupational Hygiene Society

This society will hold a conference at the London School of Hygiene and Tropical Medicine, Keppel Street, W C 1 on Monday April 4 at 11 A.M. The subject chosen for discussion is the Assessment of Health and Disease in Industry and the principal speakers will be Dr Donald Stewart Dr Robert Murray Dr Roy Archibald and Prof A Bradford Hill, F.R.S Further particulars may be had from the hon. secretary of the society M.R.C Laboratories, NW 3

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[1] Arts, 19[illegible], 102, 958

[illegible] Leprosy Relief Association 8 Portman Street

## Leeds Regional Hospital Board

*Major J C Hunter has been appointed chairman of this* board in succession to Alderman H J Bambridge, who is retiring on March 31

## Scottish Western Regional Hospital Board

Captain J P Younger has been appointed chairman of the board in succession to Sir Alexander Macgregor, who retires on April 1

## S H M O s in Birmingham Region

The Senior Hospital Medical Officers Group of this region will hold their second meeting on Saturday, March 5, at *3 P M , at Marston Green Maternity Hospital, near Birmingham*

## Army Appointment

Dr P M. Daniel has been appointed honorary consultant in neuropathology to the Army at home

## Medical Field Survey

On Tuesday, Feb 22, at the Westminster Medical School, Horseferry Road, London, S W 1, at 6 P M , Dr A L Cochrane will speak on this subject at the study circle on medical statistics of the Royal Statistical Society

## Medical Association for Prevention of War

*London Branch* —On Saturday, Feb 26, at 8 P M , at 45, Russell Square, London, W C 1, Professor Takai, who holds the chair of pædiatrics at Osaka University, will read a paper to this branch on the medical aspects of the atomic disaster in Japan

## Myxomatosis Confirmed in Hare

*The Times* of Feb 12 reports that the Veterinary Laboratory, Weybridge, has confirmed that the carcass of a hare found in Northern Ireland was affected with myxomatosis This is the first time that myxomatosis has been confirmed in a hare in the United Kingdom

## London Medical Orchestra

This orchestra still welcomes additional players The next concert will be a performance of Haydn's Passion, *The Seven Last Words*, on Good Friday Further particulars may be had from the secretary, Dr E V Slaughter, 6, Oxford Court, London, W 3

## Tuberculosis Travel Grant

The Scottish branch of the National Association for the Prevention of Tuberculosis offers a grant of £250 for postgraduate study abroad to a doctor working in the field of tuberculosis Further particulars may be had from the Scottish secretary of the association, 65, Castle Street, Edinburgh, 2, to whom applications should be sent not later than April 1

## Exhibition of Medical Drawings

At 3 30 P M on Friday, April 15, Sir Cecil Wakeley will open an exhibition of medical drawings illustrating Art in the Service of Medicine, which the Medical Artists Association of Great Britain is holding at B M.A House, Tavistock Square, W C 1, from April 16 to 30 The exhibition will be open on weekdays from 10 A M to 5 P M (Wednesdays until 8 P M )

## Pocket Money for Old People

From April 25, when the new retirement pensions become payable, residents in old people's homes will have their pocket money raised from 6*s* 6*d* to 7*s* 6*d* weekly At the same time the minimum weekly charges for board and lodging will be raised from 26*s* to 32*s* 6*d* Old people whose resources are insufficient to meet the new charges and at the same time retain 7*s* 6*d* as pocket money, will be put in funds by the National Assistance Board

At a dinner held on Feb 8, Mr A. J C Gormley, chairman of Messrs John Wyeth & Brother Ltd , of London presented to Sir Alexander Fleming, F R S on behalf of the Wright Fleming Institute of Microbiology a donation from the Wyeth organisation in Great Britain and the United States for the purchase of research apparatus

The *Quarterly Journal of Experimental Physiology* is now published by Messrs E & S Livingstone, 16 Teviot Place Edinburgh, 1 The annual subscription to the journal which is published quarterly is 3 guineas

*Guida Villit* —English doctors may obtain free copies of this guide to Italian holiday resorts and spas on application to Prof B Erba, Ufficio Stampa Medica Italiana, Via Budua 13 Milan

# Diary of the Week

FEB 21 TO 26

### Monday, 21st

HUNTERIAN SOCIETY
8 30 P M (Mansion House, E C 4 ) Mr L E C Norbury
the Time of John Hunter

### Tuesday, 22nd

BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P M (London School of Hygiene and Tropical
Keppel Street, W C 1 ) Prof A C
Metabolism
ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street W 1
8 P M *Medicine* Dr J T Ingram, Dr H J Wallace Dr
MacKenna Cutaneous Manifestations of Systemic
ST MARY'S HOSPITAL MEDICAL SCHOOL, Paddington W 2
5 P M. Prof Hugh McLaren Carcinoma of the Uterine Body
INSTITUTE OF DERMATOLOGY, St John's Hospital, Lisle
W C 2
5 30 P M Dr E J Moynahan Carcinogenesis

### Wednesday, 23rd

ROYAL SOCIETY OF MEDICINE
5 P.M *Endocrinology* Sir Stanford Cade, Sir Charles
F R S Hormones and Cancer
INSTITUTE OF DERMATOLOGY
5 30 P M Dr Henry Haber Squamous Cell Epithelioma
INSTITUTE OF DISEASES OF THE CHEST Brompton S W 3
5 P.M Sir Russell Brock Results of Mitral and Aortic
INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330 Gray's Inn
W C 1
5 30 P M Prof F C Ormerod Hoarseness
MANCHESTER MEDICAL SOCIETY
4 30 P M (Medical School ) *Medicine*. Dr C E Dent

### Thursday, 24th

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn
W C 2
3 45 P M Dr Frank Stansfeld Growth and
Bone (Arnott demonstration )
BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P M (London School of Hygiene and Tropical
Mr R A Kekwick D.SC The Plasma Proteins
INSTITUTE OF DERMATOLOGY
5 30 P.M Mr H S Williams Physical Principles of
Therapy
ROYAL SOCIETY Burlington House W 1
4 30 P M Prof Wilson Smith F R.S , Dr G Belyavin, Dr F
Sheffield Host Tissue Component of Influenza
Dr Robert Halliday Absorption of Antibodies
Immune Sera by the Gut of the Young Rat
NUFFIELD ORTHOPÆDIC CENTRE, Wingfield Morris
Hospital Oxford
8 30 P M Mr J C Scott Results of Conservative
Fractures of the Femoral Shaft
UNIVERSITY OF ST ANDREWS, Medical School, Small's
Dundee
5 P M Dr D P Cuthbertson Work of the Rowett
Institute

### Friday, 25th

UNIVERSITY OF LONDON
5 30 P M (London School of Hygiene and Tropical
Dr J H Sheldon Old Age
POSTGRADUATE MEDICAL SCHOOL OF LONDON Ducane Road, W
2 P.M Mr D Lang Stevenson General Surgical
4 P.M Dr J J R. Duthie Systemic
Rheumatoid Disease
ROYAL SOCIETY OF MEDICINE
8 15 P M *Obstetrics and Gynæcology* Prof W C W
Dr C N Smyth Dynamics of the Human
INSTITUTE OF DERMATOLOGY
5 30 P M. Dr R T Brain Precanceroses and Epitheliomata
INSTITUTE OF LARYNGOLOGY AND OTOLOGY
3 30 P.M Mr J C Hogg Dysphagia
ROYAL COLLEGE OF SURGEONS OF EDINBURGH, Edinburgh, 8
3 30 P M Mr Ian Fraser Tumours of the Small
ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF
242 St Vincent Street Glasgow
5 P M Prof Stanley Alstead Therapeutics—Tropical

# Births, Marriages, and Deaths

## BIRTHS

AMBROSE —On Feb 9, at City of London Maternity Hospital Sheila (née Clavering) wife of Dr Gordon Ambrose—a son

## MARRIAGES

DOPSON—PONSFORD —On Feb 12 at St Michael's Church, gate, Mr Laurence Dopson to Dr Joan Ponsford, senior officer at Park Hospital, Manchester

Doctors who wish to watch the Boat Race from the premises should make early application for tickets to Dept Vitamins Limited, 23 Upper Mall, London W 6

# PREVENTION AND TREATMENT OF HYPERTENSIVE HEART-FAILURE BY GANGLION-BLOCKING AGENTS *

K SHIRLEY SMITH
B.Sc M.D Lond F.R C.P
PHYSICIAN IN CHARGE OF THE CARDIAC DEPARTMENT

P B S FOWLER
B.A. D.M. Oxfd, M.R C P
ASSISTANT PHYSICIAN

CHARING CROSS HOSPITAL, LONDON

THE most common complication of hypertension is art failure That this feared and grave event is sentially the outcome of left ventricular overwork s never seriously been questioned From this assump on has sprung the conception that every effort must made to lower the blood pressure in hypertensive art-disease In recent years the introduction of nglion blocking drugs has enabled physicians to duce blood pressure surely and significantly Since art-failure is the commonest cause of death in hyper nsion, the effect of differing degrees of blood pressure ntrol on this complication needs study The pursuit steady pressure control has tended to obscure the ct that one of the essential aims of therapy is the revention of left ventricular failure We aim here to ow how this purpose may be achieved even if there is ot a continuous significant reduction of pressure and o record the changed pattern of cardiovascular com plications and mortality among hypertensive patients treated with hexamethonium

TABLE I—LEFT VENTRICULAR FAILURE TREATED WITH HEXAMETHONIUM

| ase no. | Treat-ment (mos.) | Other drugs | Improve ment in effort tolerance | Comments |
|---|---|---|---|---|
| 1 | 31 | | + + + | |
| 2 | 30 | | + + + | |
| 3 | 24 | Digitalis | + | Poor control of blood pressure |
| 4 | 18 | | + + + | Disappearance of gallop rhythm |
| 5 | 16 | Digitalis at first | + + + | Cure of severe cardiac asthma |
| 6 | 15 | Digitalis | + + | Without digitalis, dyspnœa before injections of hexa methonium |
| 7 | 12 | Digitalis | + + | Cure of cardiac asthma |
| 8 | 7 | | + + + | |

The practical aspects of the management of these patients have already been described (Smith et al 1954)

## Effect of Hexamethonium on Heart failure

In our series of 114 hypertensive patients treated with ganglion blocking agents mainly hexamethonium bro mide there were 26 in heart failure established or threatened In every case this had set in before treat ment with hexamethonium started Congestive heart failure was present in 6 established left ventricular failure in 14 and incipient left ventricular failure in 6 The results of hexamethonium treatment in these three groups were as follows:

(1) *Congestive Heart failure.*—3 patients have been followed for eighteen, eighteen, and twelve months. In each instance digitalis and mersalyl were used at first In 2 of the patients, after the disappearance of congestion hexamethonium given alone prevented the recurrence of failure The 3rd patient remained greatly better when treated with hexamethonium and digitalis than he was when given either alone 3 later patients presenting with hypertensive congestive failure were treated first with hexamethonium alone. They failed to respond to this treatment and needed digitalis and mersalyl Their follow up has been too short to say whether hexamethonium alone will prevent the recurrence of failure

(2) *Established Left Ventricular Failure*—There were 14 patients with established left ventricular failure treated with hexamethonium The results in 8 cases are summarised in table I Although all in this group have remained out of heart failure 3 have died of strokes and 2 of uræmia and another is dying in this state Hexamethonium alone brought swift relief to most of these patients and prevented recurrence even when blood pressure control was not maintained over the twenty four hours. In 1 patient paroxysmal dyspnœa came on before each of the two daily injections of hexa methonium bromide and was relieved by the subsequent injec tion digitalis prevented these attacks Of the 2 other patients requiring digitalis in this group 1 had very severe heart damage and 1 was but poorly controlled with oral hexamethonium.

TABLE II—CONTROL OF BLOOD PRESSURE AND RELIEF OF DYSPNŒA IN 18 PATIENTS PRESENTING WITH DYSPNŒA

| Control of blood pressure | Relief of dyspnœa | | | |
|---|---|---|---|---|
| | Good | Fair | Poor | Total |
| Good | 6 | 1 | | 7 |
| Fair | 3 | 2 | | 5 |
| Poor | 5 | 1 | | 6 |

(3) *Threatened Left Ventricular Failure.*—6 patients in this condition were all greatly improved by ganglion blocking agents. They had been under treatment for an average period of eighteen months. Not only was dyspnœa notably relieved but also there was alleviation of other symptoms and signs, such as angina and gallop rhythm

In all three groups of patients recurrence of heart failure appeared to be prevented by hexamethonium even when the blood pressure was poorly controlled over most of the twenty four hours In table II blood pressure control is correlated with relief from dyspnœa in 18 patients complaining solely or essentially of this symptom All had hypertensive heart-disease and had been treated with hexamethonium for one to three years The table shows that there is no relationship between alleviation of dyspnœa and lowering of blood pressure and it must therefore be assumed that even when the blood pressure control is far from continuous the treatment produces a significant effect on the cardiac condition

## Cardiovascular Complications

The total incidence of cardiovascular complications in our series is shown in table III In no case has heart failure developed during treatment with hexamethonium Attempts to relieve congestive heart failure due to hypertension by blood pressure control alone have failed, and this method of treatment cannot vie with digitalis and mersalyl in bringing swift relief although ganglion blocking agents may prevent recurrence of heart failure

TABLE III—TOTAL INCIDENCE OF CARDIOVASCULAR COMPLICA TIONS AMONG 114 HYPERTENSIVE PATIENTS TREATED WITH HEXAMETHONIUM

| Complication | No of cases | Time relation to therapy |
|---|---|---|
| Congestive heart failure | 6 | All existed before treatment |
| Left ventricular failure | 14 | |
| Incipient left ventricular failure | 6 | |
| Angina pectoris | 8 | All pre-existed ; much improved |
| Cardiac infarction | 7 | 3 before treatment 4 during (2 died) |
| Strokes | 12 | 5 before treatment 6 during (5 died) 1 before and after (died) |
| Raynaud's phenomenon Gangrene | 1 | During therapy |

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* A paper read at the Second World Congress of Cardiology in Washington U.S.A on Sept 16 1954

In our experience the existence of myocardial ischæmia by no means precluded treatment with hexamethonium In fact, when considerable hypertension was associated with angina, the control of the hypertension often brought a lessened incidence of pain Cardiac infarction had taken place in 3 cases before treatment was started Of the 4 cases of cardiac infarction occurring during hexamethonium treatment only 1 appeared to be directly related to the sudden fall of blood pressure Of the seven strokes witnessed in the course of this treatment a similar relationship was observed once

### *Causes of Death*

There were 14 deaths during the follow up period in our series The mortality was due to strokes (6) and uræmia (5), and there were 2 deaths from cardiac infarction and 1 from an unknown cause There were no deaths from heart failure These figures suggest that this therapy has caused a complete change in the mortality pattern of hypertension It appears that heart-failure is prevented, with the result that deaths from cerebral catastrophe may take place, just as insulin has reduced the coma death rate while increasing that from arterial disease There is no evidence, on the other hand, that hexamethonium treatment is attended by a special liability to either hæmorrhage or thrombosis The 2 instances already mentioned of thrombosis occurring when blood pressure was at its lowest were both treated with watery solutions of hexamethonium bromide and not with the retard preparation used in all the later cases to ensure a slower and steadier absorption 6 patients had strokes before treatment, and 1 of them had a fatal recurrence after treatment Among 8 patients with angina pectoris and 3 with cardiac infarction occurring before therapy there were no thromboses after the beginning of treatment

It has been argued that cerebral hæmorrhage is related to fluctuation in the level of blood-pressure rather than to the height of the blood-pressure itself Though hexamethonium does cause substantial alterations of blood-pressure these are less than those which the hypertensive patient undergoes as the result of physical exertion Fowler and Guz (1954) showed the protective influence exerted by hexamethonium bromide on hypertensive people during exercise It is therefore probable that fluctuations of blood-pressure during treatment with the patient up and about are less than those which might be expected without treatment

### Discussion

Gilmore et al (1952) found that the introduction of hexamethonium bromide through a cardiac catheter was followed by a fall of systemic and pulmonary arterial pressure, cardiac output being little altered It is reasonable to infer that the work of the heart was thereby lessened, and that heart-failure might be relieved and averted That this result might be achieved was shown by Kelley et al (1953), who treated patients in congestive heart failure of various types by intravenous injections of hexamethonium bromide 30 mg They found reduction in arterial pressure (and of venous pressure, if raised) and in most patients a quickened circulation time, improved vital capacity, and alleviation of symptoms, notably orthopnœa Similar results were found by Shuman et al (1954), who showed that autonomic blockade was an effective means of relieving pulmonary congestion in heart-failure In short, the changes expected during relief of congestive failure were observed

A mathematical demonstration of the reduction of the work of the heart as a result of the action of hexamethonium has been given by Johnson et al (1954), who have emphasised that hypertension often accounts for the persistence of intractable heart failure By cardiac catheterisation they have measured left ventricular work before and immediately after intravenous injectio of hexamethonium They found that left ventricula work was decreased from 182 to 46 joules per minute That the expected clinical results of such treatment hypertensive left ventricular failure may be obtain has been recorded by Smirk (1954) In 20 of 36 seve hypertensives with either congestive heart failure cardiac asthma there were relief from symptoms an return to a range of activity appropriate for their t of life In these patients such treatment was not supplemented by digitalis or mercurial diuretics or by depletion

For hypertensive left ventricular failure the bas treatment must be (1) to improve the power of the heart, (2) to ensure that the heart receives all the that advantageous circumstances can give, and (3 to lessen the work demanded of the left ventricle Und (1) digitalis should be given To secure (2) the patient should be propped up in the feet down posture of the cardiac bed, and body-fluid depletion should be secured by salt and fluid restriction The accomplishment (3) must be through lessening the pressure in the systemic circuit How effective continuous control of blood-pressure may be in this direction has already been shown It has likewise been demonstrated that a substantial lowering of blood pressure for even eight twelve of the twenty four hours may sufficiently light the work of the heart for the symptoms and signs left ventricular failure to be resolved This effect pressure reduction is so potent that it may in many ca without any additional measures, bring about drama and continuing relief from acute or chronic left ventricula failure, if this is the consequence of hypertension

### Summary

A series of 114 patients under treatment with hex methonium bromide for hypertension were studied wi special reference to the incidence and control of heart failure

It was found that this treatment could not take th place of digitalis and mersalyl in the initial treatmen of congestive heart failure, but by controlling the pressure it might prevent recurrence

If left ventricular failure existed when the patient cam under treatment it was generally relieved by hexa methonium bromide In a few cases digitalis contributed to the control exerted by hexamethonium bromide Dyspnœa lessened and cardiac asthma no longer occurred and angina and gallop rhythm, if present, disappeared.

There was no death from heart failure, which ordinarily the commonest termination of hypertensiv heart disease Among the 14 deaths, strokes and uræmia were the main and nearly equal causes

We consider that the main and attainable purpose of hexamethonium treatment is the prevention of left ventricular failure

Side effects may be formidable and demand relaxation of treatment, even so, when there is incomplete control of pressure, the main aim of preventing heart failure may still be achieved

Our thanks are due to Dr Vincent Edmunds, who allowed us to make use of data from some patients under his care at Mount Vernon Hospital, Northwood

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# AN IMPROVED METHOD FOR CLINICAL STUDIES OF TOTAL EXCHANGEABLE SODIUM

## ING $^{22}$Na AND A WHOLE-BODY COUNTING TECHNIQUE

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THE isotope-dilution technique has become an estab hed method for studies on body composition both in lth and in disease (Moore 1946) and is important in ical biochemical research (Edelman et al 1952)

The present report is confined to the determination of otal exchangeable sodium," a measurement which has en found applicable to numerous clinical problems various workers and is typical of isotope-dilution surements generally

The measurement of exchangeable sodium usually volves the use of the 15-hour half life isotope $^{24}$Na— Miller and Wilson (1953) The required figure is ived from the formula :

$$Na_E = \frac{^{24}Na\ administered - {}^{24}Na\ excreted\ in\ urine}{^{24}Na\ per\ m.eq\ \ {}^{23}Na\ in\ plasma}$$

In practice 12–24 hours is usually regarded as sufficient the $^{24}$Na to reach equilibrium with the exchangeable dium in the body ; the source of the body-sodium mple for analysis then becomes immaterial and a ecimen of urine serves the purpose

The 2 6-year half life isotope $^{22}$Na has been used for udying the biological decay rate or turnover of sodium urch et al 1947) continuous measurements of the ount of tracer excreted are made to obtain a graph body $^{22}$Na content as a function of time Burch et al 949) have shown mathematically how the intake and cretion rates, the exchangeable body-sodium and the iological decay rate are interrelated

The technique described here permits the direct easurement of the biological decay rate and serial easurements of exchangeable sodium The essential atures of the method are the use of long lived $^{22}$Na gether with an apparatus for measuring radioactivity the whole body so that in effect the numerator in the rmula above is measured directly

### Methods

*Preparation of $^{22}$Na* *

The radioactive sodium was prepared by deuteron mbardment of magnesium in the University of Birmingham cyclotron The target material was dissolved in HCl and after the addition of NaCl carrier the agnesium was precipitated as magnesium hydroxide nd magnesium ammonium phosphate The stock olution was made up to contain 20 µC of $^{22}$Na per ml of isotonic saline solution This was diluted with water for oral administration The activity was measured with a 4π Geiger Müller counter (Gray 1952)

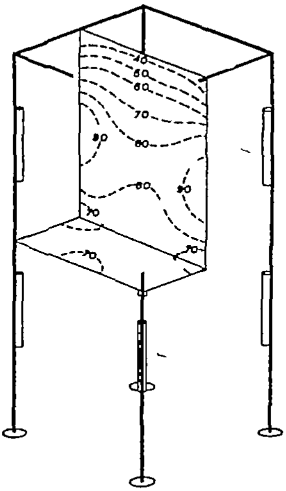

Fig 1—Schematic drawing of whole-body counting-equipment, showing lines of equal sensitivity

*Measurement of Whole body Radioactivity*

The apparatus in current use is shown schematically in fig 1 Eight gamma ray counter tubes (20th Century Electronics type G 24) are lashed to a frame in this case an ordinary hospital ward screen The tubes were matched by the manufacturers to have the same operating voltage they are connected in parallel to a Probe Unit 1014A and thence to a conventional scaler and E H T unit. Measurements made by moving a small bottle containing $^{22}$Na in two planes show a large region in the centre of the apparatus where movement of the source has relatively little effect on the counting rate The person to be examined stands in the centre as shown in fig 2. With a person of average size a dose of 50 µC of $^{22}$Na corresponds to a counting rate of about 10 000 counts per minute (c p m.) The background count in the absence of nearby artificial radioactive sources is about 800 c p m

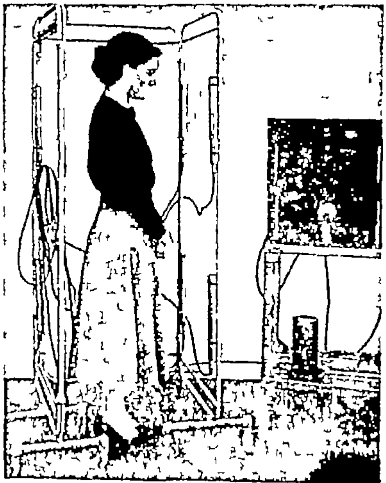

Fig 2—Whole-body counting-equipment made from screen.

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* This material is obtainable from the Atomic Energy Research Establishment, Harwell

TABLE I—CONSISTENCY OF WHOLE BODY ACTIVITY MEASUREMENTS FOR 6 HOURS

| Time (hr ) | Observed counting rate (c p m ) | Counting rate corrected for excretion (c p m ) |
|---|---|---|
| 3 7 | 21 400 | 21,400 |
| 4 0 | 21,280 | 21 280 |
| 4 15 | 21 200 | 21,380 |
| 4 6 | 21 200 | 21 380 |
| 4 65 | 20,950 | 21 130 |
| 4 9 | 21,020 | 21,200 |
| 6 45 | 21,000 | 21,180 |
| 6 9 | 21 020 | 21,200 |
| 7 5 | 21,000 | 21,180 |
| 7 85 | 20,900 | 21,200 |
| 8 25 | 20,900 | 21 200 |
| 8 65 | 20 850 | 21,250 |
| 9 35 | 21 000 | 21,300 |
| | | Mean 21 237<br>σ = ± 0 52% |

*Measurement of $^{22}$Na in Urine*

Spot urine samples are stored in small 'Polythene' bottles while awaiting measurement, to avoid errors due to exchange between $^{22}$Na and the $^{23}$Na in glass Radioactivity was measured with a liquid sample beta counter tube (20th Century Electronics type M 6) but a multitube gamma counting equipment (Veall and Baptista 1954) was later found to be slightly more sensitive, and much more convenient in practice A prototype scintillation counter for liquid samples ('EKCO' type N550) has also been tested, this is about eleven times more sensitive than the equipment using Geiger tubes, and a further increase in sensitivity is obtained if the 10-ml sample cup supplied by the manufacturer can be replaced by a larger one The radioactivity of each urine sample is compared with that of an aliquot of the administered dose, at least 10,000 counts being recorded on each sample

*Determination of $^{23}$Na in Urine*

Chemical sodium determinations are made by means of an EEL flame photometer (Evans Electroselenium Ltd ), using external standards All samples and standards are kept in polythene bottles

## Experimental

Preliminary experiments were made with 15-hour $^{24}$Na obtained from the Atomic Energy Research Establishment, Harwell These included measurements made on the whole-body counting equipment after the oral administration of $^{24}$NaCl in solution, to observe the effect of non-uniform distribution of the isotope, experiments to check the reproducibility of measurements after equilibration of the isotope, and a limited series of calibrations of the equipment made to obtain an estimate of the effect of the size and shape of the person under investigation

TABLE II—RESULTS OF PAIRED OBSERVATIONS OF TOTAL EXCHANGEABLE SODIUM FOR A HEALTHY MAN

| Days after dose | Exchangeable sodium (m eq ) | | Ratio A/B |
|---|---|---|---|
| | A | B | |
| 1 | 2950 | 3183 | 0 9296 |
| 4 | 2731 | 3059 | 0 8928 |
| 5 | 3219 | 3181 | 1 0119 |
| 6 | 3067 | 3016 | 1 0169 |
| 7 | 2932 | 2989 | 0 9809 |
| 8 | 3029 | 3034 | 0 9983 |
| 12 | 2724 | 2995 | 0 9095 |
| 13 | 3023 | 3152 | 0 9590 |
| 15 | 3109 | 3324 | 0 9353 |
| 18 | 3463 | 3352 | 1 0331 |
| 19 | 3022 | 3121 | 0 9683 |
| 20 | 3352 | 3303 | 1 0148 |
| 21 | 3026 | 3037 | 0 9964 |
| 22 | 3621 | 3562 | 1 0167 |
| | | | Mean 0 9760<br>Coefficient of variation ±4 35% |

Normal healthy people were used, they were on ordinary hospital duties, and there was no vari from their normal routine or diet About 30 µC $^{22}$Na was given orally, not necessarily with the p fasting After several hours the first measurement whole body activity was made (initial activity) corrected for urinary excretion, if any On the follow day and at intervals thereafter the whole-body count rate was measured, the bladder having been vo immediately beforehand The urine sample so obta was used for radioactivity and chemical determinat

In one case the subject was given 25 µC of $^{22}$Na. three weeks an additional dose was given each d immediately after the whole body count had been m the dose being calculated to maintain the whole-b count at a steady value Subsequently the fall in b activity was followed in the usual way

## Results

*Performance of Whole body Counter*

Immediately after the subject had taken an oral of $^{24}$Na the whole body counting rate was found t about 30% less than the equilibrium value The count rate increased with time until, after 1–2 hours, a st value was reached

Measurements of whole-body activity made over a 6 hours are shown in table I Measurements were b after sufficient time had been allowed for effecti complete equilibration The coefficient of variation single measurement, after correction for excretion, ± 0 5%, which is equal to the coefficient of var to be expected if a measurement is based on 40 counts, as these were

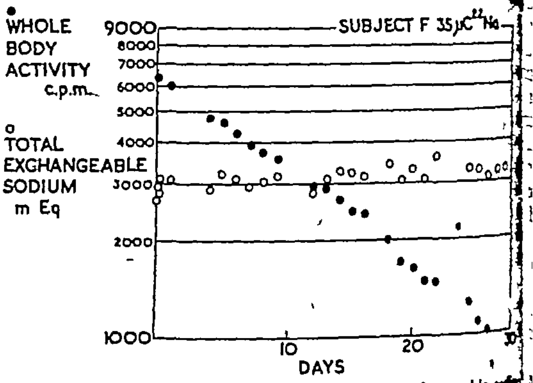


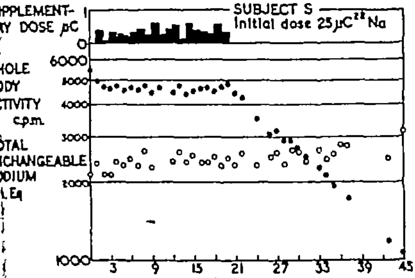
Fig 3—Whole-body activity and apparent total exchangeable after single tracer dose of $^{22}$Na.

*Accuracy of Determination of Exchangeable Sodium*

The results of pairs of measurements of exchange sodium in the same person are shown in table II Th measurements were made about 3 hours apart, usu at about 11 A M and 2 P M each day It can be seen fr the ratios in the third column that usually the interven midday meal leads to an increase of about 2 5% the amount of exchangeable sodium Even with the uncertainty regarding the intake and excretion between the two measurements the data yield a coefficient of variation for the ratio of ± 4 35%, hence the corre sponding figure for a single measurement is ± 3%

*Serial Measurements*

The whole-body activity, the specific activity of the urine sodium, and the exchangeable sodium calculated from these two quantities are shown in fig 3 for a health man after a single dose of 35 µC of $^{22}$Na The same d for another person, who received an initial dose of 25 µ and daily supplementary doses for 3 weeks thereaft are shown in fig 4



4—Whole body activity and apparent exchangeable sodium with supplementary doses of $^{22}$Na

The curve for total body activity is of the expected rithmic form the biological half life being about 11 ys This is in agreement with the results of Miller al (1954) and Burch et al (1949) The curves for hangeable sodium show an apparent slight increase h time as the $^{22}$Na is excreted

## Discussion

Immediately after an oral dose the $^{22}$Na is in the gastro stinal tract. Most of the radioactivity is thus situated the region of minimal sensitivity of the whole body nter and there is also a considerable reduction in nting rate due to the absorption of gamma radiation the rest of the body As the isotope becomes more formly distributed, the counting rate increases but is ficiently constant after 3 hours to allow a calibration re (in counts per minute per microcurie) to be obtained the person under study This calibration figure varies dely from person to person depending both on size d shape hence calibration in this way is necessary each case

From the known standard errors of the individual asurements involved, the measurement of exchange e sodium is calculated to have a standard error of 2 3% which agrees with the degree of reproducibility own in table II However measurements made from y to day on the same person show considerably wider riations than this—in most cases about ± 5% or re This is presumably due to daily variations in ake and excretion of sodium Probably the relatively de range of values for exchangeable sodium in healthy ople reported by previous workers (summarised by ons et al 1954) are due, at least partly, to these daily riations Arons et al (1954) discussing the wide range normal values suggest that changes in the electrolyte ntent of the body are likely to be of greater clinical portance than the values obtained from single observa ns The present method by reason of the frequent asurements which can be made not only permits re detailed study of short-period fluctuations but so makes it easier to discern relatively long term nds

Previous workers (Burch et al 1952, Miller et al 1954) tained results which suggest that the exchange of sodium continues at least up to 96 hours after adminis tration of the tracer By external counting over the patella Miller et al obtained direct evidence in support the suggestion that the slowly equilibrating component primarily sodium in bone On the other hand Edelman et al (1954) reported that 45% of bone sodium exchangeable in 4 hours and found no evidence of rther exchange in the next 20 hours in man or in 1 onth in dogs on a low-sodium diet

In the present experiments the apparent increase in xchangeable sodium, as the tracer is excreted, is consistent with the assumption that some of the $^{22}$Na is associated with slowly exchanging sodium in the body with the result that its excretion is delayed and the measured specific activity of the excreted sodium is lower than the average specific activity of the total exchangeable sodium The data shown in fig 4 where the effects of excretion have been largely balanced out, together with the data of Miller et al (1954) support the conclusion that about 10% of the total exchangeable sodium represented by the difference between "24 hours" exchangeable sodium and "7-days" exchangeable sodium, can be regarded as forming a separate compartment the equilibration of $^{22}$Na between this compartment and the extracellular fluid being characterised by a half life of about 2 days The mathematical theory of the distribution of a tracer substance in multi compartment systems of this type has already been discussed by Solomon (1949) After about 7 days equilibration appears to be complete That the $^{22}$Na in bone is not fixed is confirmed by the finding that in a healthy person after 75 days (7 half lives) less than 1% of the administered dose remained in the body

In studies extending over several weeks with people whose excretion of sodium is normal or near normal uncertainties in interpretation can be reduced by adopting a procedure whereby an initial dose of about 25 μC of $^{22}$Na is followed at intervals of 7–10 days by supplementary doses of about 10 μC each This avoids excessively high counting rates in the early stages and subsequently, the inordinately long measurements needed for very low counting rates The same procedure also eliminates a major source of error in the method any changes of weight or shape of the subject such as those associated with gross œdema and particularly those found in obstetrical studies will lead to appreciable changes in the calibration factor of the whole body counter The administration of supplementary doses provides opportunities for checking the calibration of the equipment. With this system of dosage the greater part of the slowly exchangeable sodium is included in the figure obtained and it is more certain that the sodium associated with cellular, amniotic ascitic and pleural fluids is included than is the case when only the 24 hour exchangeable sodium is measured

Previous workers who have studied the radioactivity of the whole body (Burch and Spiers 1953 Reines et al 1953) have been concerned with the measurement of quantities of about 0 01 μC of the naturally occurring radioactive elements This presents considerable technical problems and involves the use of complex equipment In the present case the magnitude of the dose used is determined by the amount which can be measured in samples of urine or of plasma and the building of apparatus with adequate sensitivity for the whole body radioactivity measurement presents no difficulties For instance although the limit to the sensitivity of the apparatus is set by the background counting rate, it has not so far proved necessary to use any lead shielding round the counters In the present apparatus it is also found that for practical purposes the effect of the natural radioactivity of $^{40}$K is balanced by the background shielding effect of the subject's body Thus a count taken on one person before administration of $^{22}$Na gave 10±0 c p m for the body background.

Our own unpublished data confirm the conclusion reached by Arons et al (1954) that simultaneous measurements of exchangeable sodium and potassium are probably of greater interest and value than either quantity alone The technical problems involved in the double tracer technique are greatly reduced if the method described here is used for the sodium measurements, while $^{42}$K (12 4 hour) is used in the conventional manner (Corsa et al 1950) for the potassium measurements. Owing to the widely different decay rates and radiations of and $^{42}$K the measurement of samples containing both of these isotopes is comparatively easy (Tait and Williams 1952) The use of $^{22}$Na also represents a considerable financial saving compared with $^{24}$Na, because the frequent shipments and high wastage due to radioactive decay are avoided

The main advantage of the present method lies in the fact that complete collection of all excreta is unnecessary, and the possibility of loss of sodium in sweat does not have to be considered The method thus lends itself particularly well to environmental studies Measurements on healthy volunteers are greatly facilitated, clinical studies can now be made in the antenatal and outpatient clinics instead of in the metabolic ward, and the patient is not subjected to inconvenience or to emotional stress The whole body counting apparatus is a relatively inexpensive attachment to the now widely available radioactivity measuring equipment and can be varied considerably to meet different requirements Thus it is relatively simple to adapt the apparatus for measurements on bed patients Apart from electrolyte studies, the technique is generally applicable to any problem where the absorption or retention of a gamma emitting radioactive isotope in the body is of interest

### *Radiation Dosage*

The 2 6 year half life of $^{22}$Na gives rise to some misgivings about the radiation dosage received by the subject However, the effective half life in the body is determined by the excretion rate and is about 2 weeks There is no evidence of any permanent retention The currently accepted figure for the maximal permissible radiation dose rate for continuous exposure is 0 3r per week (International Commission on Radiological Protection 1954), and the maximal permissible body burden of $^{22}$Na corresponding to this dose rate can be calculated (Mayneord and Sinclair 1953) For a person weighing 70 kg this amounts to about 50 $\mu$C In the present studies it has not been found necessary to exceed this figure at any time, and measurements were usually made at about half this activity level It therefore appears that, so far as radiation dosage is concerned, observations could be continued on the same person indefinitely

A H James (personal communication) has pointed out, however, that the possibility of the incorporation of appreciable amounts of $^{22}$Na in the " non exchangeable " bone sodium in cases where mineralisation of bone tissue is occurring has not been excluded The use of this isotope in late pregnancy with a viable fœtus, or in growing children, is thought to be inadvisable until the results of further experimental studies are known

## Summary

The fraction of a tracer dose of a gamma emitting isotope which remains in the body after a given time can be measured by a simple Geiger Müller counter system

Using $^{22}$Na this technique permits direct measurement of the biological decay-rate and serial measurements of total exchangeable sodium The biological half life for healthy people is about 11 days The standard error of a single measurement of total exchangeable sodium is ±3%

About 10% of the total exchangeable sodium takes several days for complete equilibration, uncertainties due to this and to calibration errors caused by changes in shape or size of the subject can be reduced by suitably fractionating the administered tracer dose

Body-sodium measurements may be continued indefinitely on the same person without exceeding the permissible maximum of radiation dosage figure of 0 3r a week

The technique is simple and enables studies to be made on hospital outpatients The whole body counting-technique is applicable in a wide variety of other cli
investigations

We wish to thank Mrs V Parker and Miss A W their technical assistance Part of the cost of this work covered by a grant from Messrs Bayer Products Ltd., Lond

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# LOW-FAT DIET AND THERAPEUTIC DOSES OF INSUL IN DIABETES MELLITUS

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THERE is no indication that healthy people tak a diet rich in carbohydrates are especially liable diabetes, in fact numerous observations show improvement of carbohydrate tolerance following its gre intake The Staub-Traugott effect is a classical exam of this in acute experiments As a long term ef diabetes mellitus is not especially common among th huge and mainly carbohydrate eating population the world—e g, the Chinese—except the rich and sedentary among them who partake of large quanti of fat as well and encourage obesity by overeating

Although it is theoretically possible that in s circumstances the islets of Langerhans can be exhaus there is no experimental proof that this happens. (1923) showed that the relationship between the car hydrate ingested and the insulin necessary to metabo it was approximately logarithmic, hence the strain the insulin mechanism is relatively small Moreover it impossible to improve to any great extent non hypoglycæmia by treatment for months with a di containing a very large quantity of carbohydrates

Even diabetics tolerate a high carbohydrate diet

Strouse and Soskin (1932) found that increased intake carbohydrate from 72 to 200 g in isocaloric diets of diabe did not increase the demand on insulin, and the glycos effect remained more or less the same

Jackson and Kenefick (1942) recorded similar finding in diabetic children

Rabinowitch (1949) claimed that inclusion of 20-50 g sucrose in a diabetic diet *definitely reduced* the re requirements

Soffer and Gabrilove (1951) cite a man, aged 65, who h diabetes for fifteen years and took 50-60 teaspoonfuls sucrose in various forms in addition to his normal di throughout his illness without deteriorating further in a way his insulin requirements remaining constant at 40 u of protamine zinc insulin daily This diabetic never l dosis or pyogenic infections despite glycosuria equivalent 50–60 g of glucose.

Ellis (1934) who treated some cases of severe diabetes ith 600 g. of glucose daily in lieu of restricted diet and on entical doses of insulin found that instead of deteriorating any way some of the patients showed increased carbohydrate tolerance In one case this effect was striking ler 21 days treatment the insulin requirements were duced from 192 units to 0 units daily

Fat however depresses the insulin mechanism msworth (1934 1935) confirmed the findings of earlier orkers that a high-carbohydrate diet increases sugar derance whereas a high fat diet decreases it and owed that the result was solely due to the increased nount of carbohydrates in the diet Each unit of insulin these circumstances metabolises a greater amount of ucose (see above)

Since these findings the tendency has been to abandon gh fat low-carbohydrate diets in the treatment of abetes and to give a diet containing a normal or a aller than normal amount of fat a normal amount carbohydrate and a normal amount of protein with equate insulin The findings described here suggest at if fat is reduced still further to the minimum sulin begins to exert its curative effect most patients n be stabilised progressively on diet alone and me patients are to all intents and purposes cured pparently when a diet very low in fat is given the abetogenic stimulus is minimised, and insulin in lequate amounts can then cure diabetes as has been own experimentally by Haist et al (1940) and Lukens d Dohan (1942)

## Methods

*election of Patients*

All the cases were of insulin sensitive diabetes Of the 0 patients 6 were female and 74 male and 17 were 23 lb overweight for their age height body frame d sex the remaining 63 being from normal to 45 lb derweight Except 1 child aged 13 and 2 men aged -80 the patients were aged 20–58 Ketonuria was und in 14 and glycosuria alone in 66 23 apparently d no symptoms and of the remaining 57 patients were picked up semicomatose and 55 complained of mptoms ranging from weakness to all the classical mptoms of diabetes mellitus None of them had any ptic complications

Apart from the initial glucose tolerance test on each tient it was impossible to estimate the blood sugar vel frequently because of the cost Accordingly only tients with an approximately normal renal threshold re selected for treatment to enable day to day observations to be made on the urine Where the fasting blood gar level was higher than 190 mg per 100 ml. and the rmality of renal threshold could not initially be cided, results of single blood sugar estimations and of rine examinations done two hours after a meal at intervals while the diabetic state was coming under progressive control with treatment helped to determine whether the renal threshold was normal or not The results of the initial glucose tolerance tests are given in table I to give an idea of the types of cases treated

*Diet*

The patients without ketosis were allowed unrestricted high-carbohydrate diet without insulin for the week before the initial glucose tolerance test Subsequently they were put on a diet of required caloric value for them for treatment purposes This diet contained 20–30 g of fat and 120–150 g of protein, and the rest of the caloric requirement was made up by carbohydrates excluding free sugar The caloric value was based on nergy requirements and calculated for a shift of the body weight towards 5–10 lb below normal at the rate of 2–3 lb increase in the underweight and a similar decrease in the overweight per month Apart from the patients who were grossly underweight and received as much as 4000–4500 calories a day, the caloric value of the diet in the remaining cases was 1600–2200 calories Subsequently, with improvement in the diabetic process, however many patients started losing weight on their original diets and the caloric value had to be increased accordingly There were three main meals: breakfast, luncheon, and dinner of about $^{2}/_{8}$, $^{3}/_{8}$ and $^{3}/_{8}$ of the total caloric value and given at 8 A.M. 1 P.M and 8 P.M respectively Minor variations for bed tea, afternoon tea and a bedtime drink were allowed for convenience and satisfaction of patients

TABLE I—RESULTS OF INITIAL GLUCOSE TOLERANCE TESTS

| Case no | Blood sugar (mg per 100 ml) | | | | | |
|---|---|---|---|---|---|---|
| | Fasting | After 50 g of glucose | | | | |
| | | ½ hr | 1 hr | 1½ hr | 2 hr | 2½ hr |
| 1 | 266 | 298 | 333 | 400 | 366 | |
| 2 | 192 | 201 | 258 | 333 | 289 | |
| 3 | 108 | 228 | 203 | 202 | 135 | |
| 4 | 292 | 208 | 333 | 390 | 30 | |
| 5 | 11 | 216 | 230 | 142 | 133 | |
| 6 | 100 | 238 | 254 | 153 | 111 | |
| 7 | 273 | 339 | 363 | 322 | 285 | |
| 8 | 324 | 400 | 476 | 392 | 380 | |
| 9 | 212 | 234 | 2 6 | 300 | 284 | |
| 10 | 614 | 660 | 670 | 644 | 634 | |
| 11 | 210 | 245 | 312 | 298 | 250 | |
| 12 | 102 | 350 | 312 | 306 | 288 | |
| 13 | 303 | 3 3 | 116 | 408 | 370 | |
| 14 | 190 | 250 | 296 | 322 | 307 | |
| 15 | 228 | 24 | 312 | 285 | 253 | |
| 16 | 126 | 222 | 268 | 206 | 250 | |
| 17 | 180 | 278 | 307 | 279 | 232 | |
| 18 | 439 | 454 | 370 | 400 | 328 | |
| 19 | 184 | 373 | 294 | 294 | 250 | |
| 20 | 276 | 303 | 400 | 384 | 302 | |
| 21 | 220 | 280 | 430 | 440 | 330 | |
| 22 | 173 | 272 | 31 | 254 | 18 | |
| 23 | 470 | 333 | 579 | 579 | 500 | |
| 24 | 206 | 30 | 303 | 333 | 285 | |
| 25 | 151 | 106 | 16 | 210 | 188 | |
| 26 | 285 | 230 | 330 | 390 | 289 | |
| 27 | 187 | 200 | 201 | 290 | 314 | |
| 28 | 109 | 234 | 266 | 29 | 250 | |
| 29 | 171 | 205 | 280 | 286 | 266 | 224 |
| 30 | 190 | 333 | 493 | 533 | 333 | 313 |
| 31 | 233 | 333 | 100 | 600 | 400 | 333 |
| 32 | 152 | 2 2 | 2 2 | 72 | 200 | 166 |
| 33 | 272 | 3 5 | 333 | 272 | 250 | |
| 34 | 250 | 428 | 300 | 128 | 375 | |
| 35 | 3 3 | 493 | 600 | 800 | 430 | 37 |
| 36 | 110 | 200 | 300 | 280 | 250 | 1 0 |
| 37 | 160 | 300 | 280 | 260 | 260 | 210 |
| 38 | 110 | 180 | 200 | 290 | 170 | 1 0 |
| 39 | 253 | 391 | 154 | 400 | 388 | |
| 40 | 160 | 202 | 280 | 315 | 285 | |
| 41 | 142 | 250 | 275 | 238 | 108 | |
| 42 | 230 | 312 | 317 | 281 | 217 | |
| 43 | 86 | 108 | 221 | 216 | 202 | |
| 44 | 250 | 300 | 108 | 3 2 | 333 | |
| 45 | 140 | 198 | 235 | 222 | 209 | |
| 46 | 173 | 180 | 198 | 238 | 203 | |
| 47 | 347 | 308 | 421 | 414 | 400 | |
| 48 | 123 | 258 | 370 | 285 | 205 | |
| 49 | 111 | 181 | 101 | 208 | 200 | |
| 50 | 420 | 500 | 518 | 487 | 470 | |
| 51 | 117 | 208 | 250 | 253 | 234 | |
| 52 | 116 | 500 | 371 | 512 | 487 | |
| 53 | 125 | 180 | 212 | 258 | 250 | |
| 54 | 11 | 186 | 210 | 228 | 204 | |
| 55 | 143 | 330 | 250 | 228 | 181 | |
| 56 | 212 | 307 | 120 | 400 | 3 1 | |
| 57 | 186 | 250 | 206 | 2 | 21 | |
| 58 | 115 | 173 | 290 | 228 | 168 | |
| 59 | 93 | 190 | 228 | 210 | 160 | |
| 60 | 111 | 235 | 250 | 2 8 | 192 | |
| 61 | 100 | 190 | 300 | 3 | 470 | |
| 62 | 121 | 2 8 | 275 | 258 | 200 | |
| 63 | 148 | 258 | 275 | 250 | 231 | |
| 64 | 222 | 2 0 | 390 | 317 | 370 | |
| 65 | 110 | 216 | 280 | 260 | 209 | |
| 66 | 138 | 190 | 233 | 258 | 228 | |
| 67 | 119 | 180 | 221 | 222 | 218 | |
| 68 | 216 | 296 | 160 | 35 | 334 | |
| 69 | 125 | 280 | 273 | 200 | 142 | |
| 70 | 600 | 726 | 800 | 858 | 1000 | |
| 71 | 125 | 212 | 206 | 255 | 80 | |
| 72 | 86 | 201 | 235 | 275 | 228 | |
| 73 | 150 | 230 | 333 | 80 | 210 | |
| 74 | 172 | 181 | 210 | 212 | 2 2 | |
| 75 | 97 | 186 | 2 5 | 218 | 168 | |
| 76 | 8 | 161 | 238 | 212 | 1 | |
| 77 | 111 | 163 | 213 | 202 | 161 | |
| 78 | 128 | 232 | 222 | 2 2 | 160 | |
| 79 | 135 | | | | | |
| 80 | 320 | | | | | |

*Method of Administration and Dosage of Insulin*

The patients who had been on diet for 7–10 days and still had glycosuria were put on relatively large doses of insulin calculated to leave a slight excess after counteracting the glycosuria completely The initial dose of insulin was approximately determined by allowing a unit of insulin for each gramme of glucose excreted in the urine in twenty four hours and adding 5–10 units of extra insulin to this amount This dose counteracted the glycosuria in most cases except the severest, which needed somewhat higher doses

Calculated in this way the initial dose of insulin was between 30 units in milder cases to 120 units in the severer ones, and was given as protamine zinc insulin half an hour before breakfast When the patient had been free from glycosuria for 48–72 hours the dose of insulin was reduced by 5–10 units till the patient was sugar-free again for the same length of time This was repeated till either no insulin was required or the minimal dose of insulin had been reached This procedure, which progressively increased carbohydrate tolerance, was applied to 10 patients, who became just sugar free on diet alone They received 20 units of protamine zinc insulin initially to be reduced by 5 units every five days till none was to be given

TABLE II—FINAL RESULTS OF TREATMENT IN 7 CASES

| Case no | — | Blood sugar (mg per 100 ml) | | | | | |
|---|---|---|---|---|---|---|---|
| | | Fasting | After 50 g of glucose | | | | |
| | | | ½ hr | 1 hr | 1½ hr | 2 hr | 2½ hr |
| 1 | Initial | 260 | 296 | 333 | 400 | 360 | |
| | Final | 90 | 172 | 156 | 115 | 92 | |
| 24 | Initial | 266 | 307 | 363 | 333 | 285 | |
| | Final | 90 | 126 | 160 | 97 | 96 | |
| 44 | Initial | 250 | 360 | 408 | 372 | 333 | |
| | Final | 90 | 148 | 160 | 153 | 142 | 100 |
| 79 | Initial | 435 | Not done patient had severe ketosis | | | | |
| | After 9 weeks | 168 | 177 | 204 | 209 | 190 | 157 |
| | Final | 103 | 180 | 165 | 146 | 113 | |
| 80 | Initial | 520 | Not done patient had severe ketosis | | | | |
| | After 9 weeks | 114 | 172 | 212 | 208 | 180 | |
| | Final | 88 | 170 | 177 | 167 | 101 | 76 |
| 48 | Initial | 123 | 258 | 320 | 285 | 205 | |
| | Final | 108 | 206 | 258 | 210 | 120 | |
| 68 | Initial | 210 | 296 | 400 | 357 | 333 | |
| | Final | 128 | 210 | 190 | 175 | 150 | |

There was never any danger of excessive dosage of insulin The initial amounts given were only slightly above the doses which counteracted glycosuria completely Reduction by 5–10 units at a time subsequently within a few days generally allowed some glycosuria after one or more meals before being controlled again Hypoglycæmic reactions were further avoided by adequate spacing, in time and quantity, of meals It will be noticed that the caloric values of luncheon and dinner were the same, and dinner was late This helped to prevent trouble from nocturnal hypoglycæmia even when the initial dose of protamine zinc insulin was 120 units

Urine was tested for glycosuria before breakfast and two hours after breakfast, luncheon, and dinner every day. All the samples had to be sugar free for 48–72 hours before the insulin dosage was reduced

## Results

Of the 80 patients 50 became sugar free in 3–6 weeks and did not require any more insulin, and 14 (cases 8, 13, 21, 27, 31, 34, 39, 44, 47, 52, 56, 64, 68, and 73) showed slight irregular glycosuria on some days and not on others, which could be controlled adequately with 10 units of protamine zinc insulin Of these 14 pati 8 (cases 8, 13, 21, 34, 47, 52, 56, and 68) impro subsequently and did not require any insulin b weeks, and the remaining 6 (cases 27, 31, 39, 44, 64, 73) continued to show irregular glycosuria

TABLE III—VARIATIONS IN GLUCOSE TOLERANCE ASSOCI WITH INTAKE OF FAT

| Date | Blood-sugar (mg per 100 ml.) | | | | | |
|---|---|---|---|---|---|---|
| | Fasting | After 50 g of glucose | | | | |
| | | ½ hr | 1 hr | 1½ hr | 2 hr | 2½ hr |
| Oct 10 1949 | 520 | Not done, patient had seve ketosis | | | | |
| | | After very low fat diet | | | | |
| Dec 18 1949 | 114 | 172 | 212 | 208 | 180 | |
| Feb 9 1950 | 100 | 140 | 180 | 160 | [illegible] | [illegible] |
| March 9, 1950 | 110 | 165 | 190 | 150 | 12[illegible] | [illegible] |
| April 10, 1950 | 112 | 175 | 180 | 170 | 150 | [illegible] |
| June 17 1950 | 96 | 140 | 165 | 110 | 95 | [illegible] |
| July 7 1950 | 86 | 115 | 145 | 120 | 80 | [illegible] |
| Aug 9, 1950 | 90 | 105 | 130 | 95 | 90 | |
| | | After indiscretion with fats | | | | |
| Sept 9 1951 | 160 | 380 | 280 | 250 | 200 | [illegible] |
| | | After reversion to very low fa diet | | | | |
| Sept. 20, 1951 | 115 | 220 | 260 | 210 | 160 | [illegible] |
| Sept 23, 1951 | 67 | 120 | 137 | 129 | 101 | [illegible] |
| | | With 50–60 g of fat | | | | |
| April 28 1952 | 78 | 153 | 167 | 172 | 166 | [illegible] |
| May 5, 1952 | 88 | 170 | 177 | 167 | 101 | [illegible] |

Case 31 agreed to undergo treatment with œstrogen the in spite of the risks and was given 25 mg of stilbœstrol alternate days for 3 weeks He became considerably wo and œstrogen had to be stopped He was re treated with d and insulin for 4 weeks before he could be restored to t original state

10 patients (cases 5, 6, 38, 43, 59, 60, 75, 76, 77, and who became sugar free on diet alone (see above) sho considerable increase of carbohydrate tolerance af 20 days' insulin treatment They acquired an additio reserve of 150–400 calories

The 6 patients with severe diabetes (cases 10, 18, 50, 61, and 70) initially required 80–120 units of protami zinc insulin, but at the end of 6 weeks they could controlled with 20–40 units After 18 weeks' treatm they still required about the same or a smaller amou

All these cases have been followed up on diet alone f from 6 months to 5 years Because of the cost involve as already pointed out, it was only possible to do ser glucose tolerance tests subsequently in 7 patients (case 24, 44, 48, 68, 79, and 80) In 18–26 months 5 of th (cases 1, 24, 44, 79, and 80) have returned to well wit normal and for all purposes are apparently cured Th now take fat more liberally, but it is limited to 50-60 daily The remaining 2 patients (cases 48 and 68) ha

TABLE IV—VARIATIONS IN GLUCOSE TOLERANCE CURVES

| Date | Blood sugar (mg per 100 ml) | | | | | |
|---|---|---|---|---|---|---|
| | Fasting | After 50 g of glucose | | | | |
| | | ½ hr | 1 hr | 1½ hr | 2 hr | 2½ hr |
| Oct 10 1952 | 435 | Not done, patient had severe ketosis | | | | |
| Dec 23 1952 | 140 | Not done patient had myo cardial infarction | | | | |
| Jan 8 1953 | 167 | Ditto | | | | |
| Feb 27 1953 | 168 | 177 | 204 | 209 | 190 | 1[illegible] |
| April 17, 1953 | 110 | 140 | 161 | 188 | 167 | 16[illegible] |
| May 15, 1953 | 134 | 168 | 195 | 187 | 162 | 111 |
| July 7 1953 | 130 | 184 | 185 | 151 | 108 | |
| Sept 12, 1953 | 123 | 180 | 174 | 146 | 00 | |
| Oct 3, 1953 | 110 | 202 | 165 | 155 | 109 | |
| Nov 18, 1953 | 121 | 184 | 167 | 123 | 106 | |
| Dec 12, 1953 | 123 | 189 | 169 | 120 | 97 | |
| Feb 6 1954 | 126 | 172 | 207 | 172 | 138 | |
| April 17 1954 | 121 | 186 | 166 | 135 | 71 | |
| May 15 1954 | 116 | 184 | 174 | 148 | 102 | |
| July 9, 1954 | 111 | 102 | 173 | 153 | 110 | |
| Aug 6 1954 | 103 | 180 | 165 | 146 | 113 | |

ucose-tolerance curves suggesting very mild diabetes he results obtained in these 7 cases are summarised table II

In addition there is an interesting 8th case a woman w aged 37 whose initial records have been lost In ecember, 1950 she required initially 20 units of pro mine-zinc insulin After 8 weeks treatment she quired none. After nearly 4 years of continuous low fat et she has turned up with hypoglycæmic symptoms and glucose-tolerance curve of fasting 59, $^1/_2$ hr 71 1 hr 90 $^1/_2$ hr 110 2 hr 88 and 2$^1/_2$ hr 70 mg per 100 ml

The results in these 8 cases are significant In the t case with hypoglycæmic symptoms it appears that e diabetic tendency has been lost There is evidence om records of case 80 (table III) that, unless the low fat t is kept up for a long time the diabetic tendency appears; but it can be recontrolled

The glucose-tolerance curves undergo the following anges of improvement (1) lowered fasting sugar ) reduced hyperglycæmia with delayed fall (3) moderate perglycæmic reactions, and (4) within normal curves. ese changes may be more or less progressive (table III) may show slight variations from time to time (table IV)

With the return of glucose tolerance to normal in the ng run there was a concomitant fall in blood-cholesterol vel

With improvements in symptoms the glycosuric ndition and general health in a short space of 3–6 eks, most patients did not mind the comparatively ght inconvenience of adjusting themselves to the w fat diet and were fully coöperative

## Summary

80 patients with insulin-sensitive diabetes were treated th low fat optimal caloric diets containing 20–30 g fat, 120–150 g of protein, and the rest carbohydrate d progressively diminishing therapeutic doses of insulin 50 of them became sugar free in 3–6 weeks and 8 in weeks and did not need any more insulin 6 needed units of insulin daily and in 6 cases the original quirement of 80–120 units was reduced to 20–40 units 7 cases were checked with serial glucose-tolerance tests r 18–20 months 5 of them showed return to normal d 2 to almost normal Another case in which poglycæmia developed is described

10 patients who had become sugar free on diet alone wed increased carbohydrate tolerance

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The most obvious characteristic of present-day ndards is their *tentative and uncertain nature* and the ree of variation observable within quite small groups in the population The official mores to which the individual ght turn for guidance are far from clear in relation to such matters as marriage divorce sex relations, and parenthood and the various sources of authority differ greatly among themselves. The modern individual finds himself in a painful dilemma. On the one hand he feels himself to be under no very rational compulsion to obey any one set of rules or observe any particular customs On the other hand he is not convinced that these rules and customs have no validity and especially if he finds himself in trouble is likely to feel at least some guilt for having infringed them He is at once unwilling to accept external rules and unhappy over the consequences of accepting responsibility for his own decisions "—Social Casework in Marital Problems FAMILY DISCUSSION BUREAU London: Tavistock Publications. 1955; p 164

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# MYLERAN IN CHRONIC MYELOID LEUKÆMIA

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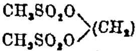
'Myleran' (1 4 dimethanesulphonyloxybutane)



$$\begin{matrix} CH_3SO_2O \\ CH_3SO_2O \end{matrix}\Big\rangle(CH_2)_4$$

(*Haddow and Timmis 1953*) is an effective palliative in chronic myeloid leukæmia (Galton 1953a and b Bollag 1953, Hansen 1954 Turesson 1953 Wilkinson 1953, Petrakis et al 1954) In its ability to relieve symptoms to reduce the size of spleen and liver, and to improve the blood picture, particularly the hæmoglobin level, it compares well with radiotherapy, and has the advantages of ease of administration and freedom from side effects Myleran is ineffective in acute leukæmias and in chronic myeloid leukæmia in myeloblastic relapse Previous reports have described short-term observations We now record the effects of repeated courses of myleran and of maintenance therapy in chronic myeloid leukæmia

### Clinical Material

The trial was started in September 1950 31 patients, including the 19 already reported (Galton 1953a), had begun treatment by March 1954 Table I and fig 1

TABLE I—METHODS OF ADMINISTRATION OF MYLERAN IN 31 PATIENTS WITH CHRONIC MYELOID LEUKÆMIA

| — | Courses of myleran only | Maintenance therapy after one or more courses | Maintenance therapy only | Total |
|---|---|---|---|---|
| Myleran only | 5 (1*) | 2 (1*) | 5 | 12 |
| Previous X rays P or drugs other than myleran | 9 (4*) | 4 (2*) | 6 | 19 |
| Total | 14 | 6 | 11 | 31 |

* More than 1 course

show the types of myleran therapy used in new patients and in those previously treated by X rays urethane, nitrogen mustard or $^{32}P$

### Dosage

Administration is by tablets of 2 mg and 0 5 mg In August 1951 we gave up the 'short intensive' courses of treatment in which 100–150 mg was given in 1–6 days, because severe bone marrow depression fatal in 1 case occurred in 3 patients The standard dose for adults has since been 0 06 *mg per kg of body weight daily* (about 4 mg ) An initial loading dose of 20 mg was used a few times (fig 4) but was found unnecessary The first 20 patients received one or more courses of myleran 8 died within a year of the only course 7 having received 'short intensive therapy 11 patients received 1–3 subsequent courses (0 06 mg per kg of body weight daily) maintenance therapy (0 5–4 0 mg daily) was eventually given to 6 of them In 11 other patients maintenance therapy was given immediately after an initial period on standard dosage

### Interrupted Therapy

Treatment was stopped when the clinical and hæmatological improvement seemed to justify it, or when the leucocyte-count was thought to be falling too steeply, which usually happened when dosage was excessive or was not adjusted according to the rate of fall With 0 06 mg per kg of body-weight daily the treatment lasted 3–7 months Subsequent treatment was deferred until symptoms returned, the leucocyte count often rose before this, and the high Hb levels reached were rarely maintained after 6 months, but in the absence of symptoms these were not regarded as indications for resumption of treatment Symptoms reappeared 5–18 months later One patient remained well for 3 years after the only course of treatment and then symptoms and signs insidiously appeared which were indistinguishable from those of polycythæmia vera (Galton 1953a, case 5)

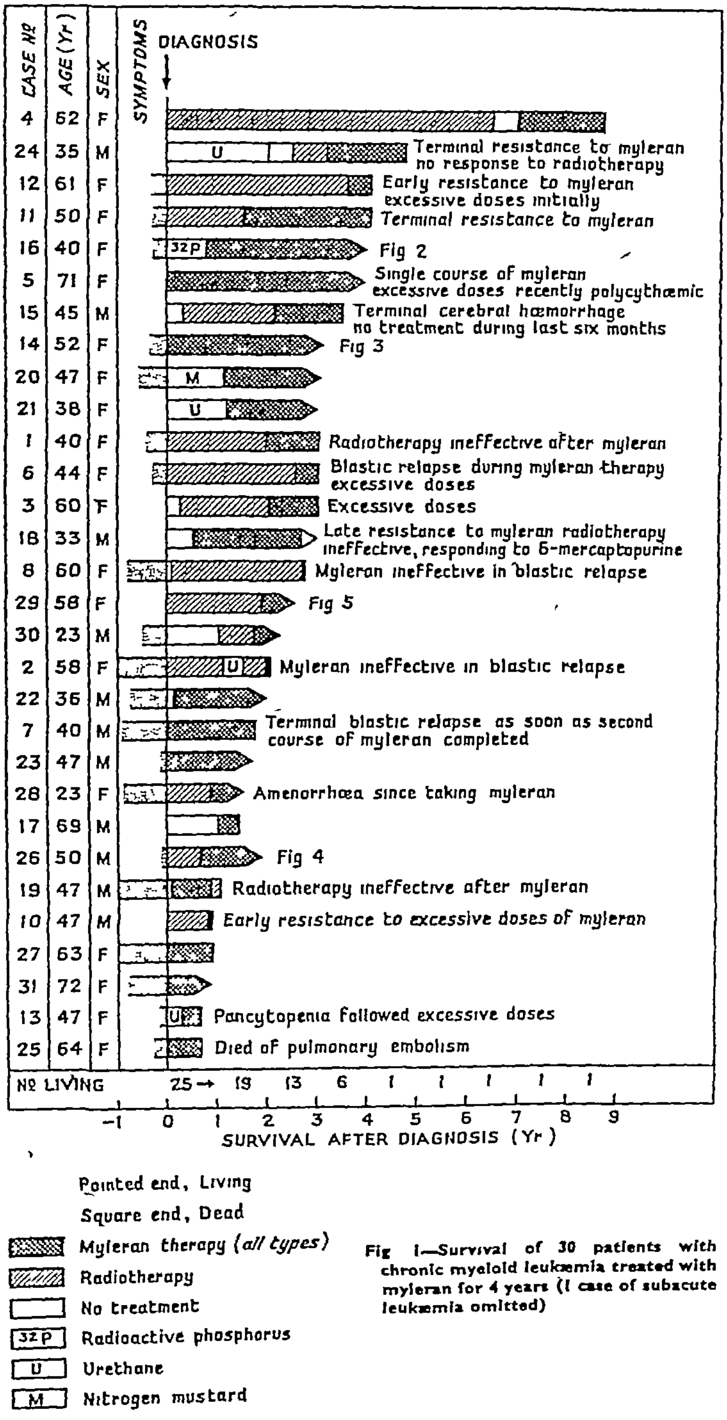


**Fig 1—Survival of 30 patients with chronic myeloid leukæmia treated with myleran for 4 years (1 case of subacute leukæmia omitted)**

### Maintenance Therapy

Remissions following second and third course of myleran were usually shorter, none exceeding 1 year (fig 2) After completion of treatment the leucocyte count rose more rapidly and heralded a quicker fall of Hb level and return of symptoms In 6 patients, therefore, the next clinical relapse was treated by attempting to reduce the leucocyte-count to 10,000–20,000 per c mm and to maintain this with appropriate doses of myleran 11 more patients who had not had myleran previously were also treated thus Treatment was begun with 0 06 mg per kg of body-weight daily, and the dose was later halved Adjustments of 0 5 mg daily were made at intervals according to the leucocyte count

### Regulation of Dosage

At each outpatient attendance the Hb level, platelet and total leucocyte counts, and absolute numbers of total immature myeloid cells were plotted The top third of the chart is printed in cm and mm squares for Hb, the rest being 4 cycle semilogarithmic paper for the platelet and leucocyte counts, which rise and fall approximately logarithmically A 50% fall in leucocyte-count reflects the same myleran activity whether the initial count is 40,000 or 400,000 per c mm. On the semilogarithmic chart the falls are parallel, but on squared paper they look flatter and might lead to unnecessary reduction of the dose of myleran Conversely, similar rising counts may not receive the attention they merit

The doses required for maintenance vary from patient to patient, and in the same patient at different times The smallest maintenance dose used was 0 5 mg daily and the largest 6 mg daily (0 065 mg per kg of body weight) No patient has yet received continuous therapy for longer than 23 months, but the development of specific resistance to myleran in 3 patients suggests that it will not be effective indefinitely

### Results

The general impression already reported has been amply confirmed Symptoms were rapidly relieved, the Hb level rose steadily, splenic regression, though somewhat slower than with radiotherapy, was equal in extent, and absolute and differential leucocyte-counts approached normal There were no side effects and thrombocytopenia, formerly thought to be an occasional hazard with therapeutic dosage, developed only once since doses exceeding 0 06 mg per kg of body-weight daily have been avoided The immediate response to second courses was similar to the first response, but the subsequent relapse came earlier

**Case 16** (fig 2)—A married woman, aged 4 complained of lassitude, tiredness, and abdominal discomfort for several months Her spleen was moderately enlarged, and a blood count on Oct 1950, showed leucocytes 105,000 (neutrophils 56,000, immature myeloid cells, 24 000) per c mm $^{32}P$ 3 5 mC given on Dec 11, 1950, produced some improvement Symptoms returned in July 1951, the spleen was again large, and on Sept 1 1951, a blood count showed Hb 82%, leucocytes 125,000 (neutrophils 52,000, immature myeloid cells 58,000) per c mm, and platelets 180,000 per c mm

*Treatment and Progress*—Myleran 6 mg daily was given from Sept 19 to Nov 30, 19 total 420 mg in 70 days Symptoms d appeared, the spleen became impalpable,

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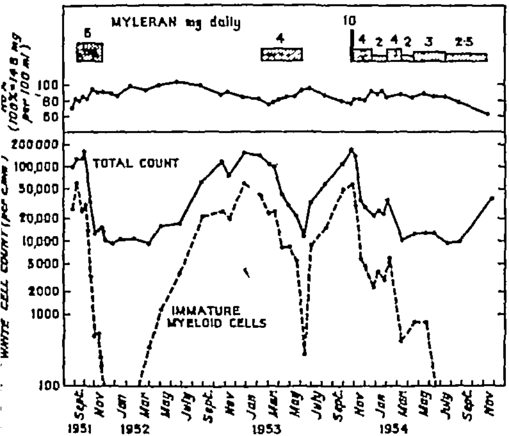
* Immature myeloid cells include metamyelocytes a earlier forms



ig. 2—Blood-counts in case 16; a patient treated with two courses of myleran and later with maintenance therapy

atient remained well. On Feb 20 1952 a blood count showed Hb 98% leucocytes 10 600 per c.mm (no immature cells) and platelets 180 000 per c.mm. The patient relapsed in December 1952 A second course of myleran 4 mg daily was given from Feb 12 to June 10 1953 (total 456 mg in 14 days) with the same result A blood-count on June 10 53, showed Hb 92% and leucocytes 11,500 (neutrophils 100 immature myeloid cells 280) per c.mm By Oct 28 53, symptoms had returned, the spleen was palpable at the level of the umbilicus and a blood-count showed Hb 75% and leucocytes 170 000 (neutrophils 84 000 immature myeloid cells 56,000) per c.mm Myleran 10 mg daily was given for week 4 mg daily for 7 weeks, 2 mg daily for 10 weeks, 4 mg daily for 4 weeks, 2 mg daily for 4 weeks and 3 mg daily for 14 weeks. On July 28 54, the patient was well her spleen was just palpable on inspiration, and a blood-count showed Hb 82% leucocytes 000 per c.mm. (no immature cells) and platelets 310,000 per c.mm The dose was reduced to 2.5 mg daily In October 1954 myeloblastic relapse supervened.

This patient had relapsed 4 months after completing her second course of myleran but remained well on maintenance therapy for a year

Case 14 (fig 3 table II).—A married woman, aged 52 complained of malaise weakness and tiredness since March 1951 In June she had pain over the left lower ribs for 3 weeks In July her spleen was found to be firm and moderately enlarged and a blood-count on Aug 2 1951 showed Hb 76% leucocytes 150 000 (neutrophils 99,200 immature myeloid cells 41 400) per c.mm., and platelets 360 000 per c.mm.

*Treatment and Progress*—Myleran 150 mg was given on Aug 3 1951; 50 mg on Aug. 26 and 27 8 mg daily from Aug 28 to Sept 25; 10 mg daily from Sept 26 to Sept. 29; and 4 mg daily from Sept 30 to Oct. 2, 1951 On Nov 6 the patient was well, her spleen was impalpable and a blood-count showed Hb 118% and leucocytes 18 000 (neutrophils 14 000 immature myeloid cells 880) per c.mm She remained well till January 1953 when all symptoms had returned and the spleen was palpable at the level of the umbilicus. On Jan 12 1953, a blood-count showed Hb 68% and leucocytes 290 000 (neutrophils 125 000 immature myeloid cells 105 000) per c.mm. The patient was given myleran 4 mg daily from Jan. 13 Subsequent adjustments of dosage and their effects on the leucocyte-count are shown in table II The patient was last seen on Oct 26 1954 in good health Her spleen was just palpable on deep inspiration and a blood-count showed Hb 91% and leucocytes 13,300 (immature myeloid cells 2400) per c.mm.

This patient has enjoyed excellent health on continuous therapy In cases 14 and 16 the spleen did not extend below the level of the umbilicus before the initial treatment and became impalpable or only just palpable with each course of myleran grossly enlarged spleens usually regressed less with each subsequent course

## HÆMATOLOGICAL CHANGES

### *Leucocytes*

Under treatment with myleran 0.06 mg per kg of body weight daily the leucocyte count was approximately halved monthly In 4 cases administration had to be stopped because the count was allowed to fall too low (5000–6000 per c.mm) No harm resulted and the counts rose No serious leucopenia developed with doses of 0.06 mg per kg of body weight or less The subsequent trend of the leucocyte-count varied in patients whose treatment was stopped when the clinical and hæmatological condition was at its best In 1 case the leucocyte-count and differential count remain normal after nearly 4 years (Galton 1953a case 5) Most patients after their first course of myleran whether or not they had been treated previously by other means showed a slow but steady increase in their total leucocyte-counts and immature leucocytes had usually reappeared in the blood within 6 months In most but not all of these

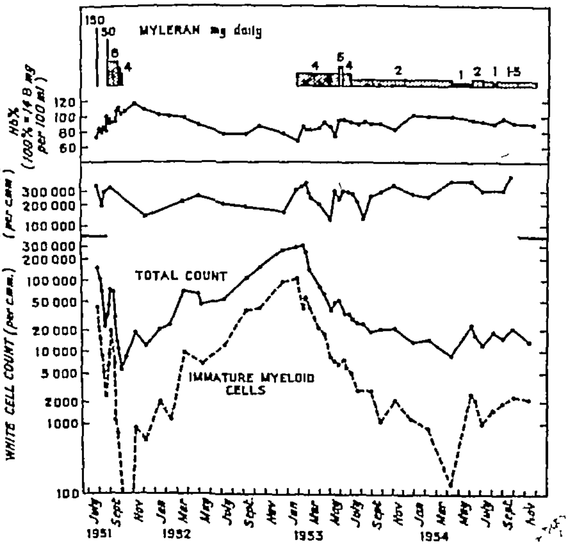


Fig 3—Blood-counts in case 14; a patient treated with one course of myleran and with maintenance therapy

TABLE II—CONTINUOUS MYLERAN THERAPY IN CASE 14 WITH CHRONIC MYELOID LEUKÆMIA, SHOWING ADJUSTMENTS OF MAINTENANCE DOSE WITH CHANGING LEUCOCYTE COUNT

| Period | Dose of myleran (mg ) | | Leucocyte-count per c.mm | |
|---|---|---|---|---|
| | Daily | Total | Initial | Final |
| Jan 13–June 30, 1953 (169 days) | 4 | 676 | 300,000 | 28,500 |
| July 1, 1953–March 9, 1954 (252 days) | 2 | 504 | 28,500 | 8800 |
| March 10–May 4, 1954 (56 days) | 1 | 56 | 8800 | 24,000 |
| May 5–June 1, 1954 (28 days) | 2 | 56 | 24,000 | 12,400 |
| June 2–November, 1954 (continuing) | 1 5 | 228 + | 12,400 | 13 300<br>Oct 26,1954 |

patients immature leucocytes had disappeared from the blood by the end of the course

The leucocyte-counts of patients treated with myleran for the second or third time fell as rapidly as they had before but the absolute number of immature leucocytes usually remained higher Soon after the end of the course the total leucocyte-count rose In some patients treated for the first time with myleran the leucocyte counts fell slowly and the numbers of immature leucocytes remained relatively high In these patients also the leucocyte-count rose quickly when treatment was stopped In both groups maintenance therapy was attempted The behaviour of the leucocyte count under maintenance therapy was closely related to the dose of myleran (figs 2 and 3, table II) When Hb increase was satisfactory we did not try to lower the leucocyte count further In cases 24 and 29 it remained between 50,000 and 60,000 per c mm for 6–18 months

*Throughout the illness the absolute immature myeloid*-cell count remained high when the spleen remained large, and fell as the spleen regressed

### *Hæmoglobin*

Although the leucocyte count is a sensitive index to the activity of myleran, the Hb level is a more valuable guide to its efficacy

Hb increase continuing for 12–20 weeks and maintained for various periods is a regular occurrence with myleran therapy The Hb level has risen in all but 1 case, in which transfusions given elsewhere masked a possible spontaneous increase (case 31), 2 cases of myeloblastic relapse (cases 2 and 8), and 1 case now regarded as one of subacute leukæmia (case 10)

In all the remaining cases Hb increase has been one of the main beneficial effects of myleran therapy Some increase was usually evident a month after the beginning of treatment, and normal levels were reached in about 12 weeks The Hb level sometimes continued to rise for another 2 months The most anæmic patients showed the most rapid increase One patient had required blood-transfusions every 6 weeks for over a year before the start of myleran therapy but needed no more afterwards, and the Hb level rose subsequently to 85%, where it stayed for 18 months (case 24) Patients who had relapsed after an initial course of myleran usually showed rather less Hb increase with subsequent courses The mean Hb increase following the first course of myleran therapy in 6 patients was 45% in 106 days (max 66%, min 18%), and after second courses in the same 6 patients was 29% in 113 days (max 46%, min 20%) In 10 patients the daily rise of Hb level was 0 40–0 62% for 12–20 weeks In 2 radio resistant patients (figs 4 and 5) the Hb level continued to fall for 6 weeks and 4 months after myleran therapy was begun

It is difficult to compare the effect of maintenance therapy on the Hb with that of an initial course of myleran, since maintenance therapy was usually started late in the course of the disease, but satisfactory H levels were maintained for long periods, in case 14 betw 80 and 120% for 23 months

Rapid Hb increase was usually, but not alw associated with rapid splenic regression, with myle therapy splenic regression was often slower than w radiotherapy, yet the rate of Hb increase was simila reticulocyte crises sometimes heralded the rise of H level We therefore believe that the Hb increase is r *and not an artefact resulting* from falling plasma volu (Berlin et al 1950) but we have not determined to erythrocyte-volumes

### *Platelets*

Dangerous thrombocytopenia has not developed s small doses have been used. Of 14 cases 7 showed significant changes in the platelet-count, 3 showed sl falls, and 4 showed slight increase in the first 12 we *treatment Only 1 of the patients* (*Galton* 1953a, case 1 on continuous therapy, who had been thromboc penic from the beginning, showed temporary pla depression during treatment, and this might have b avoided had a platelet-count been made at the prev visit

### MYLERAN AND THE "RADIO RESISTANT" PATIE

It is always difficult to claim that a drug is effec in the radio resistant case, because "radio resistanc has several meanings Several patients were referred myleran therapy because radiotherapy had been ab doned or not even tried The reasons given inclu anæmia, poor general condition, and thromboc penia, and in 1 case the presence of 8% myelobl had led to a diagnosis of acute leukæmia These patien gravely ill and thought to be beyond treatment, respond well to myleran but might have responded equally w *to properly* administered *radiotherapy* In other pati remissions induced by X rays were becoming sho lived or were short lived from the beginning In th patients myleran produced benefit that radiother could not offer In this sense, myleran is effective in t *radio-resistant case*

**Case 26** (fig 4) —A man, aged 50, complained of tiredn and irritability at work since December, 1952 On exami tion (Dr N Sacks) his spleen was just palpable A bloo count on March 25, 1953, showed Hb 65% and leucocy 193,000 (neutrophils 82,000, immature myeloid cells 58,0 per c mm. Radiotherapy to the spleen was followed by r improvement, but by August, 1953, symptoms had recur and the blood picture was the same as before treatm A second course of radiotherapy was given in August September, 1953, with good results On Oct 1, 1953, a bloo count showed Hb 88% and leucocytes 8800 (neutrop 6200, immature myeloid cells 430) per c.mm , but on Nov 1 1953, the leucocytes numbered 68,000 (neutrophils 37,00

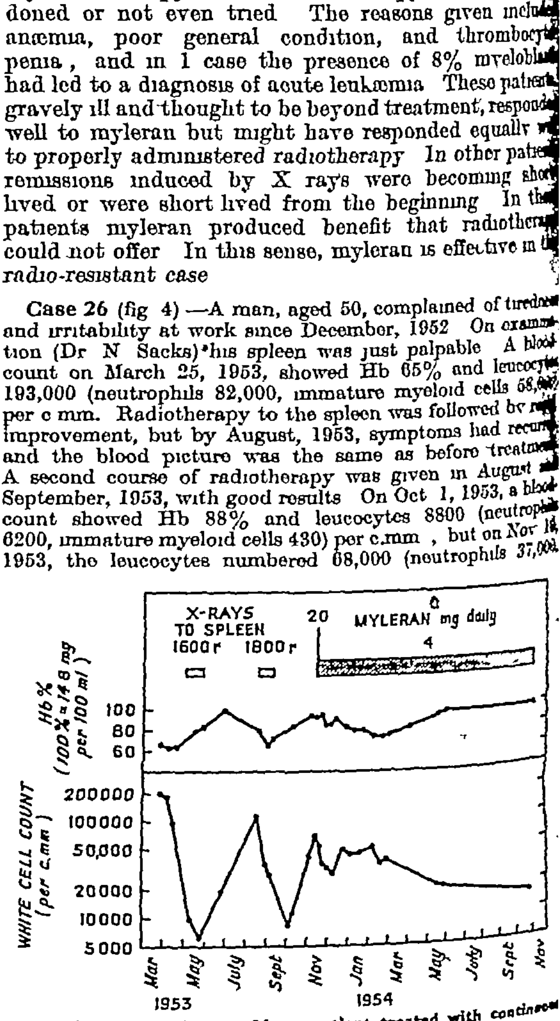


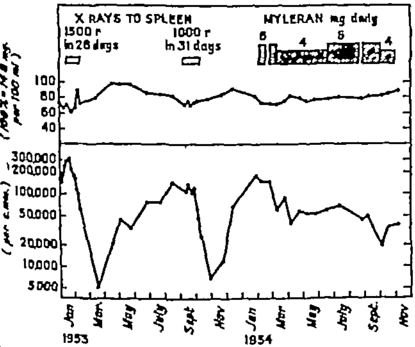
Fig 4—Blood-counts in case 26, a patient treated with continuo myleran therapy after two courses of radiotherapy

mmature myeloid cells 23 000) per c.mm. The spleen was ot palpable but there were no other relevant physical signs nd no symptoms

*Treatment*—Myleran 20 mg was given on Nov 3 1953 and om Nov 4 onwards he has been taking 4 mg daily His ealth has remained good and he has been able to travel xtensively in connection with his work. In November 1954 blood-count showed Hb 94% and leucocytes 16 100 (2400 mmature myeloid cells) per c.mm.

This was the only case in the series in which myleran herapy was begun in the absence of symptoms but crease in leucocytes from 8800 to 68,000 per c mm 6 weeks suggested that clinical relapse was impending he patient is well after a year on continuous myleran herapy

Case 29 (fig. 5)—A widow aged 58 complained of failing eight, failing memory loss of weight thirst polyuria nd deafness since December 1951 At another hospital she as found to be diabetic and hypertensive (blood pressure 0/110 mm. Hg) and her spleen and liver moderately enlarged leucocyte-count in March 1952 was 53 900 per c mm. mmature myeloid cells 30%) Her symptoms were relieved y radiotherapy a diet, and insulin In January 1953 she lt extremely ill her spleen and liver were again enlarged nd a blood-count on Jan 6 1953 showed Hb 72% and ucocytes 144,600 (immature myeloid cells 55 000) per c.mm.



g. 5—Blood-counts in case 29; a patient treated with continuous myleran therapy after three courses of radiotherapy (first course not charted)

Radiotherapy to the spleen was followed by improvement but in September 1953 another course was necessary On Dec 10 the Hb was 92%. In January 1954 the spleen was increasing in size and giving rise to pain the Hb level was falling and the leucocyte-count was rising A blood-count on Feb 1 1954 showed Hb 81% and leucocytes 180 000 (immature myeloid cells 62,000) per c.mm

*Treatment*—Myleran 6 mg daily (0 095 mg per kg of body-weight) was given from Feb 2 to Feb 16 1954 and from Feb 24 to March 10; 4 mg daily from March 11 to June 16; and 6 mg daily from June 16 onwards The patient's condition improved and apart from an attack of bronchitis in May and intermittent diabetic symptoms she has remained well. Her spleen regressed 7 cm. After myleran therapy was begun, the Hb level continued to fall for 6 weeks. On March 10 it was 72%. On Nov 2 1954 a blood-count showed Hb 87% and leucocytes 30 000 per c.mm

Remissions following radiotherapy were short lived particularly the last on myleran the patient has been well for nearly a year and the blood picture is still slowly improving In cases 26 and 29 the slow rate of fall of leucocyte-count and the delay before the Hb level began to rise should be noted

### RESISTANCE TO MYLERAN

After large doses of myleran 3 patients became rapidly resistant to further treatment with myleran (Galton 1953a) With the small doses since used this has not occurred but 3 patients with relatively stable blood pictures during continuous therapy for over a year showed slowly progressive splenic enlargement, which gave rise to pain and distension in 2 cases Myleran was withheld, and radiotherapy to the spleen was given with little effect One patient responded for a time to 6-mercaptopurine, the other 2 died At necropsy extensive leukæmic infiltration was found Thus resistance to myleran possibly specific eventually develops and may limit the period of useful therapeutic response Two other patients entered the terminal phase while on continuous therapy Their spleens were only slightly enlarged and the first indication of relapse was a falling Hb level and a rising leucocyte-count W Bollag (personal communication) obtained a response to methylcolchicine in a similar case a further short course of myleran was ineffective but a second response to methylcolchicine ensued

## Interrupted and Maintenance Therapy Compared

The *advantages of interrupted therapy* are as follows

(1) Smaller quantities of myleran are required

(2) The patient feels that something positive has been achieved when his treatment ends and he continues well for a year or more

The *disadvantages of interrupted therapy* are as follows

(1) The high Hb levels reached are not usually maintained After about 6 months an insidious fall begins leading imperceptibly to loss of fitness and efficiency before the return of definite symptoms

(2) Remissions are shorter with each successive course

(3) Patients with rapidly progressive leukæmia may relapse quickly when myleran is withheld

The *advantages of maintenance therapy* are as follows

(1) High Hb levels are maintained for long periods

(2) Good general health and high working efficiency are maintained

(3) Maintenance therapy is often successful after the remissions following interrupted courses have become short lived, or in patients with rapidly progressive leukæmia who relapse quickly after a completed course

The *disadvantages of maintenance therapy* are as follows

(1) The patient realises that he is still not normal

(2) Resistance to myleran is eventually acquired

Bone marrow failure as a result of long-continued administration of myleran was our chief apprehension when we began maintenance therapy but it has not appeared

## Routine Use of Myleran

Most patients can be treated as outpatients from their first visit Monthly attendance is sufficient when not more than 0 06 mg per kg of body weight daily is given but to observe the effect of stopping treatment or of reducing the dose two or three fortnightly visits may be necessary At each attendance the patient is weighed and examined skin and mucosæ are inspected for evidence of hæmorrhage and the sizes of spleen and liver measured in cm from fixed reference points are recorded Before therapy is begun the Hb level total and differential leucocyte-counts and platelet count (by a wet method) are determined At subsequent visits the Hb level and total leucocyte counts are plotted on a graph (see above) before further myleran is prescribed Platelet-counts and differential leucocyte-counts are not essential if a stained blood film is examined provided that the initial platelet-count is not below 200 000 or above 800 000 per c mm When the platelet-
800 000 per c mm. or higher we advocate treat
even in the absence of symptoms Both
whose platelet-counts exceeded 1 000
developed persistent priapism

The clinical response to myleran usually precedes improvement in the blood picture, but, even when the response is delayed and the Hb level continues to fall, it is worth persisting with treatment at the same dosage for as long as 4 months (case 26, fig 4 and case 29, fig 5)

## Discussion

In assessing the place of myleran in the management of chronic myeloid leukæmia we must ask first if it is an effective substitute for the best available treatment, radiotherapy (including the use of radioactive phosphorus), secondly, if it is effective when radiotherapy has failed, and thirdly, how it compares with other chemotherapeutic agents

Only 11 patients have been treated with myleran alone, 7 of whom are still living, only 2 have been observed for more than 3 years from diagnosis, which is about the median survival from diagnosis in patients treated by external radiation and with radioactive phosphorus (Lawrence 1954) It is therefore too early to compare the survival rates of patients treated with myleran alone with those treated by radiotherapy alone Thus, until statistical analysis becomes practicable, we cannot advocate myleran as a first line of treatment, although at present it appears to be a satisfactory substitute for radiotherapy and can justifiably be used as such if radiotherapy is unavailable, impracticable, or contra-indicated The absence of side-effects, though an advantage over external radiotherapy, is also the main advantage of radioactive phosphorus (Lawrence 1954) We are on more certain ground in considering patients who have responded badly to radiotherapy from the start or whose remissions have become progressively shorter These have responded well to myleran, and one might reasonably expect to prolong life

Myleran is superior to urethane, benzene, and arsenic because there are no side-effects, response is less erratic, and the remissions are longer We have not used triethylene melamine (2 4 6 tris-ethylene imino-1 3 5 s triazine) in chronic myeloid leukæmia, but usually the published results that are counted as successes seem poor by the standards we have become accustomed to since myleran became available (Bond et al 1953)

Concerning methods of using myleran, there are advantages and disadvantages of both interrupted courses and of continuous therapy Interrupted courses are often successful at first, but some patients, particularly those who relapse rapidly after radiotherapy, require maintenance therapy after the first course, and most patients require it after the second Resistance to myleran apparently specific, has developed during the second year of continuous therapy in 3 cases It is still too early to say whether continuous therapy should be deferred on this account until interrupted therapy has been tried first

## Summary

In a 4-year trial 31 patients with chronic myeloid leukæmia were treated with myleran

Successive courses and continuous maintenance therapy were used

Re treatment after courses was deferred until symptoms returned

Remissions following subsequent courses were shorter than after the first

Patients on maintenance therapy were kept well for periods up to 2 years, but resistance, apparently specific, appeared in 3 cases

Although, on limited experience, myleran is a satisfactory substitute for radiotherapy, its chief advantage is its efficacy when radiotherapy has been of limited value or has ceased to be effective

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# POSTOPERATIVE MEMBRANOUS TRACHEOBRONCHITIS

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TRAUMATIC lesions of the trachea following gene anæsthesia by intubation are relatively rare The cases considered here were felt by us to be worth recording because of their clear cut and dramatic clinical appearance and the doubt about their ætiology and patholog

## Case-reports

**Case 1**—A woman, aged 21, with pulmonary tuberculos and cavitation in the left upper lobe, underwent left upp lobectomy on July 23, 1953, from which she recove uneventfully On Aug 20, 1953, a four rib corrective thora plasty was done The anæsthesia in both cases was wi thiopentone, curare, and nitrous oxide and oxygen through cuffed endotracheal tube

Twenty four hours after the second operation the patient was very dyspnœic, flushed, anxious, and pyrexial (101°F) and had clinical and radiological evidence of collapsed le lower lobe Bronchoscopy was undertaken under local anæsthesia, and the left main bronchus was found to be obstructed by two cuffs of membranous material each about 1 cm long These were removed, and there followed immediate re aeration of the left lower lobe

*Pathology*—The material was mucinous exudate with numerous inflammatory cells enmeshed in it

**Case 2**—A woman, aged 32, with pulmonary tuberculosis, was subjected to left upper lobectomy with simultaneous corrective thoracoplasty on Dec 17, 1953 The anæsthesia was given as in case 1 At routine postoperative bronchoscopy a red œdematous circumferential area was seen at the lower end of the trachea

Forty eight hours later the patient was distressed, and her breathing was difficult and noisy, and she was flushed, anxious, and pyrexial (101°F) Bronchoscopy was immediately done under general anæsthesia, and a circumferential cuff of membrane, which was almost obstructing the lumen of the lower end of the trachea, was removed with forceps Recovery was then uninterrupted

**Case 3**—A boy, aged 12 years, was admitted to the thorac surgical centre as an urgent case on Dec 29, 1953, with tropharyngeal abscess, which had that day been unsuccess- lly explored elsewhere under general anæsthesia using a ffed tube Stridor and distortion of the trachea had en present before and after this operation, and hurried onchoscopy had been done at the end of it

On admission, twenty four hours later the trachea was -examined through the bronchoscope and, in addition to stortion due to the abscess, a circumferential white slough as seen 2 inches beyond the larynx and was thought to incide with the site of the cuff of the cuffed tube It was ot disturbed the lumen being adequate.

The abscess was drained through the left side of the neck nd two hours later urgent bronchoscopy was necessitated by vere respiratory obstruction and massive collapse of the ght lung It was found that the tracheal slough had become tached and had occluded the right main bronchus It was moved, and recovery followed.

**Case 4**—A boy aged 9 years, underwent resection of the sal segments of the left lower lobe for bronchiectasis on ept. 8 1954 The anæsthetic was generally similar to that ed in the previous cases and a cuffed tube was used

Next day the boy was very breathless and anxious his spirations being wheezy and rapid. There was radiological vidence of patchy atelectasis of the right lung Aeration of he right lung improved with postural drainage and physiotherapy but on the following day the boy was clearly much orse. He had severe stridor laboured rapid respirations orexia, and cyanosis.

Bronchoscopy under general anæsthesia showed that the pper part of the trachea immediately below the larynx was most completely obstructed by a loose circumferential embrane which on removal was found to be a cylinder em. long This produced most satisfactory clinical improve ent and radiography immediately after the bronchoscopy howed re-expansion of the collapsed segments. The clinical provement was maintained for about twelve hours, and hen renewed wheezing and distress for twenty four hours ecessitated further bronchoscopy The cylindrical membrane ad re-formed, and its removal once again brought relief This appened twice more at intervals of twenty four hours, but t the fourth and last bronchoscopy the membrane was mewhat thinner The child's further convalescence was neventful.

*Pathology.*—The cast consisted of fibrinous material showing moderate admixture with polymorphs.

### *Discussion*

It is inviting to suppose that these membranes were oughs of the mucosa, and that they had been produced by pressure necrosis at the site of the cuff of the endotracheal tube Muir and Straton (1954) point out that his has been assumed by numerous workers

Microscopy of the membranes removed in cases 1 and 4 showed no evidence of mucosal elements and, although we have no evidence of the structure of the membrane in cases 2 and 3 their very close similarity of appearance probably justifies our belief in a similar morphology

Certainly in case 1 the damage was not produced by pressure, because the membrane was found in the left main bronchus.

Belam and Zuck (1953) seem to suggest that the pressure exerted by the cuff of an endotracheal tube on the mucosa is the same as the pressure required to inflate the cuff This is clearly not so because most of this inflationary pressure is expended against the elasticity of the rubber cuff and will vary according to its strength Muir and Straton (1954) point this out and show experimentally that the pressure applied to the mucosa in the presence of a gastight fit is very small being only a few centimetres of water and well below the capillary blood-pressure

On the other hand, it is clearly possible to inflate the cuff unwittingly with much more air than is required merely for a gastight fit, and such indiscriminate inflation may produce a higher pressure on the mucosa Where hypotension is occasioned either by design or as a result of blood loss and trauma the capillary blood pressure may fall below the pressure of the cuff on the mucosa

On the whole we feel that in the average case the cuff of the tube does not produce damage by pressure; but it may well be locally traumatic if it moves within the trachea, and perhaps rotatory movements as when the head is moved from side to side, are especially important

The membranous tracheobronchitis in each of the present cases has been diagnosed fortuitously by bronchoscopy which of necessity, is a common place postoperative procedure in a thoracic surgical unit

We wonder how often membranous tracheobronchitis follows endotracheal anæsthesia for major operations on other parts of the body and masquerades as 'postoperative chest."

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# POST-PREGNANCY OSTEOPOROSIS

## A SYNDROME ?

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GENERALISED rarefaction of the skeleton is usually due to osteomalacia or osteoporosis In Western Europe, osteomalacia is usually due to steatorrhœa; but in the East, where dietary vitamin D is barely adequate it is commonly precipitated by the mineral demands of pregnancy and lactation (Snapper 1949) The pathognomonic radiological feature of osteomalacia is the Milkman fracture (or Looser's zone) and the characteristic biochemical changes are a reduction in the product of the serum-calcium and serum phosphate concentrations and a rise in the serum alkaline phosphatase

In contrast to osteomalacia, osteoporosis is primarily a disorder of the protein matrix of bone (Albright and Reifenstein 1948) It is not associated with any known disturbance of serum biochemistry, although the serum phosphate level in large series is said to be in the upper range of normal (Albright and Reifenstein 1948 Donaldson and Nassim 1954) It may occur in malnutrition thyrotoxicosis Cushing's syndrome, acromegaly or scurvy or it may present without obvious cause This latter form of osteoporosis is seen more commonly in women than in men, is usually classified arbitrarily into postmenopausal and senile varieties according to the age and sex of the patient and tends to affect the spine more severely than the rest of the skeleton. On the rare occasions when it afflicts young adults who are otherwise in good health it is known as idiopathic osteoporosis

During the past three years we have seen four young married women with backache and compression fractures of one or more vertebræ all of whom were suffering from idiopathic osteoporosis Their first symptoms appeared during or shortly after pregnancy and the purpose of this report is to suggest that the association between the osteoporosis and the pregnancy may not be fortuitous

### Clinical Histories

**Case 1**—Mrs. A a housewife was admitted in July 1952 at the age of 28 for investigation of backache and osteoporosis of the spine She had taken thyroid extract gr 3 daily for obesity from her 18th to her 24th year At the age of 22 after an uneventful pregnancy and delivery she developed lumbar backache and pains in both thighs which became so severe that about 4 months after delivery she was scarcely able to walk. Investigation elsewhere at that time revealed rarefaction of the spine associated with normal

TABLE I—SUMMARY OF HISTORY AND PHYSICAL AND RADIOLOGICAL FINDINGS

| Case | Age (years) and parity at onset | First symptoms | Breast feeding | Height (in ) | Span (in ) | Weight (lb ) | X rays | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | Codfish vertebræ | Vertebral compression | |
| 1 | 22<br>para 1 | Lumbar back ache and pain in thighs commenced 2 – 3 months after delivery | All babies breast fed for at least 3 months | 59 | 64 | 123 | + | D 12 | Limb bones normal No Milkman fractures |
| 2 | 32<br>para 2 | Lumbar backache commenced 2 months after second delivery | | 59 | 59 | 128 | + | D 6<br>D 8<br>L 1<br>L 2 | |
| 3 | 24<br>para 3 | Lumbar backache* commenced soon after third delivery | | 62 | 67† | 124 | + | D 12 | |
| 4 | 35<br>para 2 | Lumbar back ache and pain in thighs commenced 3 months after second delivery | | 67 | 71 | 150 | + | L 1<br>L 2<br>L 3 | |

* Apart from a brief episode following trauma in her first pregnancy
† Estimated from scale photograph.

calcium, phosphate, and alkaline phosphatase levels in the serum She was given calcium, calciferol, and a plaster cast, and she improved slowly, but she was still troubled by severe backache when she came to Hammersmith Hospital in July, 1952 Her recovery has continued and she is now at work, although the X ray appearances remain virtually unchanged

**Case 2**—Mrs B, a housewife who had had a normal pregnancy and delivery in 1949, was admitted in January, 1953, at the age of 32, 4 months after her second pregnancy The pregnancy had been uneventful, but 2 months after it she developed increasingly severe low back pain Radiography showed spinal osteoporosis with vertebral wedging, and she was admitted for investigation Her symptoms soon improved spontaneously, but she was given testosterone, œstrogens, and a spinal brace (Fisher type), which was discarded 12 months later When last seen in June, 1954, she was symptom free and carrying out her full duties as a housewife

**Case 3**—A Persian lady, aged 28, was admitted in August, 1953, for investigation of spinal osteoporosis There was no relevant family history, and her childhood and menarche had been normal She first noticed backache in the last month of her first pregnancy in 1947, but this resolved soon after delivery She had an uneventful second pregnancy and delivery in 1948, but her third pregnancy the following year was complicated by intermittent backache, and soon after delivery she was admitted to hospital in Tehran where the radiological and biochemical findings led to a diagnosis of idiopathic osteoporosis Her backache improved somewhat under treatment with hormones and calcium injections, but was still present occasionally when she came to London in 1953 She was given a testosterone implant and oral œstrogens and was virtually symptom free when last seen

**Case 4**—Mrs C, a housewife, aged 35, was first seen in November, 1952, at the West London Hospital, with an [illegible] week history of severe backache beginning 4 weeks after second delivery Her first pregnancy in 1949 had been complicated by toxæmia She was found to have sev spinal osteoporosis, with "codfish" deformities and vertebral compression, and normal serum biochemistry In the absence of any other predisposing cause, idiopathic osteoporosis was diagnosed Spontaneous improvement followed rapidly but the patient was subsequently given a short course of methyl-androstenediol *She is now symptom free*

The principal data from the case histories are summarised in table I All four patients gave a clear of the onset of symptoms during or just after There was nothing to suggest any of the known ca osteomalacia or osteoporosis

## Examination and Investigations

*Physical Findings*—Abnormal physical findings w confined to limitation of spinal flexion and tenderness the lower dorsal and upper lumbar spinous proce Case 1 also had a kyphoscoliosis The patients presen none of the features of Cushing's syndrome or o endocrine disorder, and they were all well nourish In three of them the span appreciably exceeded the heig and in one (case 2) span and height were equal (table

*Radiographic Appearances*—In all four cases there w extensive rarefaction of the spine, with biconca deformities (codfish vertebræ) and crush fractur (fig 1) The skull, long bones, and hands all appear normal There were no Milkman fractures

*Biochemistry*—The serum calcium and phosphate levels were normal in all patients at all times The serum alkaline phosphatase was slightly raised in case

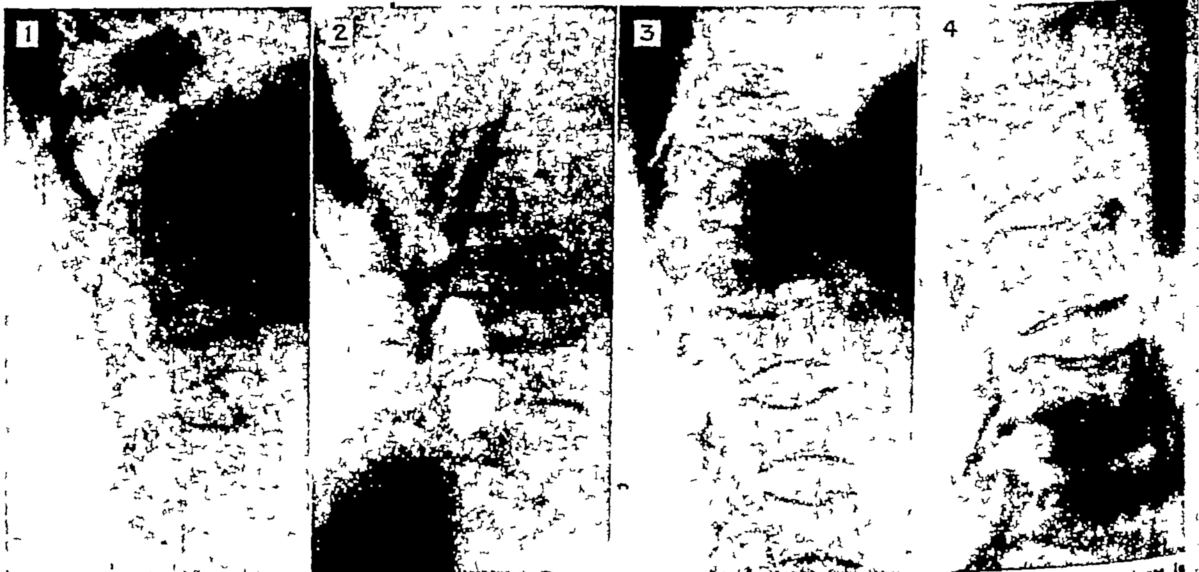

Fig 1—Lateral views of the vertebral column in the four patients showing "codfish" vertebræ and one or more crush fractures in every case.

TABLE II—PRINCIPAL BIOCHEMICAL FINDINGS

| — | | Serum | | | Urine | | Calcium tolerance test |
|---|---|---|---|---|---|---|---|
| Case | Period after delivery | Calcium (mg /100 ml ) | Phosphate (mg /100 ml ) | Alkaline phosphatase (K A units/100 ml ) | Calcium on 100 mg /day intake (mg /24 hr ) | Ratio of phosphate to creatinine clearance | 0–12 hours calcium excretion |
| 1 | 4 years | 9 8 10·0 | 3·6 3 4 | 5 5 6 0 | 140 mg (mean of 5 days) | 0 13† | |
| | 6 years | 10 0 | 2 8 | 6 7 | 75 mg | 0 10 | 57 % |
| 2 | 4 months | 9 9 10·7 | 4 5 4 1 | 18 15 5 10 0 | 220 mg (mean of 6 days) | 0 17 | 70 % |
| | 18 months | 9 6 | 3·0 | 12 1 | 48 mg | 0·11 | 81 % |
| 3 | 4 years | 10 3 | 4 3 | 11 3 | 73 mg | 0 13 | 5, % |
| 4 | 3 months | 10 6 11·0 | 3 6 4 0 | 7·0 | | | |

* Normal range about 40–60 % † Phosphate/inulin clearance.

The ratio of phosphate clearance to inulin or creatinine clearance (Milne et al 1952) was measured and found to be normal in cases 1, 2, and 3 (table II) In cases 1, , and 3 the following additional investigations were made all with normal results blood-count serum albumin and globulin, serum-electrolytes and urinary 17 ketosteroid excretion

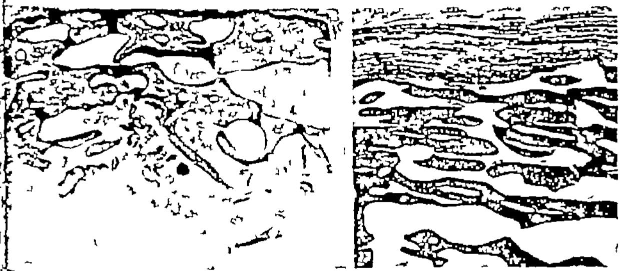

Fig. 2—Bone removed from iliac crest in cases 1 and 2 showing thin fractured trabeculæ with no osteoid seams. (Periosteal surface at the top.) (Picro-malachite × 20.)

*Metabolic Data*—Fat balances were carried out in cases 1 and 3 and yielded normal results (94% and 97% absorption) In case 4 the fat content of a single stool sample was reported as 16% of the dry weight—also normal. Urinary calcium excretion on a 100 mg calcium diet was measured in case 1 (4 years post partum) and case 2 (6 months post partum) The former excreted 140 mg daily during a 5 day period the latter 220 mg daily during a 6-day period but the figures had fallen below 100 mg when the patients were seen 2 and 1 years later respectively In case 3 (4 years post partum) the patient excreted 37 mg of calcium in the urine on the same low-calcium diet (table II)

*Calcium Infusions*—Cases 1 2, and 3 were given standard calcium infusions (Nordin and Fraser) (Normal people excrete in the urine 40–60% of the administered calcium in the 12 hours following the infusion ) In case 2 the excretion 6 months post partum was 70% and a year later 81%. In cases 1 and 3 normal percentages of the dose were excreted 6 and 4 years post partum (table II) These findings are all compatible with a diagnosis of osteoporosis and strongly against one of osteomalacia.

*Bone Biopsies*—Bone was taken from the iliac crest in cases 1, 2 and 3 (Sacker and Nordin 1954) (figs. 2 and 3) Osteoporosis (thin fractured trabeculæ) was present in cases 1 and 2 but in case 3 (4 years post partum) the biopsy specimen appeared normal No widening of the osteoid seams characteristic of osteomalacia was seen in any biopsy

## Discussion

It is tempting to attribute the skeletal rarefaction in these four patients to the increased calcium requirements of pregnancy and to regard the condition as a form of osteomalacia comparable to that which may be precipitated by pregnancy in Asiatic countries But there was nothing in the patients histories to suggest inadequate intake of calcium or vitamin D and the absence of decalcification and pseudofractures in the limb bones, despite the codfish vertebræ pointed to a diagnosis of osteoporosis rather than osteomalacia The normal serum biochemistry and the normal phosphate/inulin and phosphate/creatinine clearance ratios (Milne et al 1952) were also against a diagnosis of osteomalacia, as were the relatively high urinary calcium excretion in cases 1 and 2 on a low calcium diet and the results obtained with the calcium tolerance test

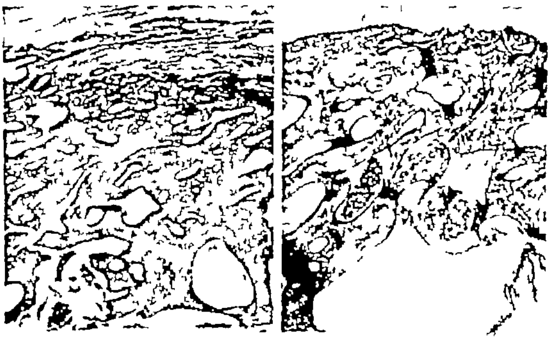

Fig 3—Bone removed from iliac crest of normal person and in case 3 thickness of cortex with that shown in fig 2. (Picro-malachite ×

In the absence of any of the recognised causes of osteoporosis, these cases would normally be classified as idiopathic However, since all four patients developed the condition in close association with childbirth, and have been improving steadily ever since, we suspect that there may be some connection between the condition and childbearing This suspicion is strengthened by the relative frequency with which idiopathic osteoporosis (though a rare condition) has been reported after pregnancy Thus, of four cases of idiopathic osteoporosis reported by Albright and Reifenstein (1948) two were young women whose symptoms first appeared soon after parturition Vaughan Jones (1953) records a case of vertebral crush fractures after eclamptic fits in a patient whose spinal radiographs show the biconcave deformity of the vertebral bodies which is seen in osteoporosis Gossler (1953) has described a case of idiopathic osteoporosis in pregnancy, Burrows and Graham (1945) have reported a case, and Devenish (1954) has seen another It must be remembered that osteoporosis cannot be diagnosed with certainty by radiography until it has reached an advanced stage, earlier stages would not be easily recognised unless deliberately sought but they might account for some of the backache which is so common during and after pregnancy Perhaps also the cough fractures in late pregnancy described by Paulley et al (1949) are manifestations of the same process

It is not easy to explain this apparent association between pregnancy and osteoporosis, but it may prove to be related to the increase of adrenocortical activity during pregnancy (Bayliss et al 1955). Osteoporosis is seen in Cushing's syndrome, and may be yet another point of similarity between Cushing's syndrome and pregnancy

As our patients have been observed for only a short time, and the period since delivery differed in each case, our data provide little information on the course of the condition We are inclined to think, however, that an acute decalcifying process began during or shortly after pregnancy (case 2), and 4–6 years later the condition was less active in the sense that symptoms were slight and the urinary output of calcium was normal (cases 1 and 3) We cannot be sure what effect, if any, hormone therapy has had upon the patients

## Summary

1 In four patients with backache due to spinal rarefaction and compression fractures, the onset of symptoms was related to pregnancy

2 In each case it was established that the condition was osteoporosis and not osteomalacia, and the term "post-pregnancy osteoporosis" is suggested for the syndrome

3 The high level of circulating plasma corticosteroids in pregnancy is invoked as a possible explanation of post pregnancy osteoporosis

We wish to thank Dr Russell Fraser, Prof G Bull, Dr L P Laurent, and Mr Charles Gray for allowing us to study their patients

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# DRUG-INDUCED ENTERITIS

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STAPHYLOCOCCAL enterocolitis is not a new disea but it now appears in a particularly virulent form as complication of "broad spectrum" antibiotic therap Several cases of fatal and non fatal drug resista staphylococcal enterocolitis have been reported in th country in the past year We wish to record this lat case following *terramycin (oxytetracycline) therapy*, t reinforce the warnings given in recent issues of this journ that the tetracycline group of drugs must be used wi care and discrimination. It illustrates the rapidity wi which drug resistance may develop, and the fulminatin nature of the attack when the patient is already weake by severe illness

## Case-record

A man, aged 33, was admitted on Oct. 20, 1954, and ruptured gangrenous appendix was removed (D W S) Aft the operation he received, twice daily, penicillin 300,0 units and streptomycin 0 5 g by intramuscular injection.

### *Course of Illness*

The patient had a postoperative ileus, but by Oct. 29 (nin postoperative day) bowel function was restored sufficient to allow gradual discontinuation of the gastric suction a parenteral fluids Progress was not maintained, however, a on Nov 1 (twelfth day) a diagnosis of small bowel obstructi was made He now had a petechial rash over his abdomen a flanks

At laparotomy (Prof W A. Mackey) the abdomen w found full of grossly distended coils of small bowel. T distension was mainly due to foul, yellow fluid and only to very minor extent to gas Widespread retroperitone hæmorrhages of purpuric type involved the posterior abdom nal wall and the lower part of the small bowel mesente The obstruction appeared to be largely mechanical, for o of the distal coils of bowel was adherent at several points an abscess in the anterior part of the abdominal cavity ju above the pelvis This abscess contained foul, thick, whit yellow pus The pus was evacuated, and the adhesions brok down Thereafter the bowel was emptied of about five pi of foul fluid by aspiration through a gall bladder trochar a cannula '*Achromycin*' (*tetracycline*) *1 0 g* in saline soluti was introduced into the cavity and the incision was closed layers

For eleven days the patient had had 600,000 units of penicill and 1 0 g of streptomycin per day In view of the severity his illness, the presence of intraperitoneal pus, and the nece sarily extensive intra abdominal manipulations, it was co sidered advisable, pending a bacteriological report on the pu to substitute for these two drugs a broad spectrum antibioti *Dissolved in a litre of Hartmann's solution*, oxytetracycli hydrochloride 0 5 g was infused twice daily, and ascorb *acid 200 mg twice daily was also given intravenously*

Immediately after the operation the patient's conditi appeared satisfactory, but during the night he becam restless and confused, and complained of a choking sensatio Next day (Nov 2) he had frank tetany (serum-calciu 4 3 m eq per litre, alkali reserve 35 0 m.eq ) This was effe tively treated with calcium gluconate 20 ml intravenousl followed by ammonium chloride given through an indwelli gastric tube in ten hourly doses of 2 5 g dissolved in 150 m of water As the blood showed deficiency of prothrombin a factor VII, vitamin K 50 mg was given intravenously T patient was also given a single intramuscular injection anti gas gangrene serum 2 ml, and started on 'Becosyn' and 2 (riboflavine 4 mg, aneurine hydrochloride 10 mg pyridoxine 4 mg, and nicotinamide 40 mg) daily b intramuscular injection

On Nov 4 there had been considerable improvement T patient was bright and talkative, and was taking flu mouth with apparent enjoyment The tongue was clean bowels were acting well, and he appeared to be in fluid ance The intravenous drip was discontinued and gastric tion gradually stopped He had had three days of tetracycline hydrochloride intravenously (1 0 g per y) and this was now replaced by 250 mg six hourly by uth

During the night his condition deteriorated and on Nov 5 was toxic and dehydrated with a choleraic appearance He o complained of a sore throat and had passed greenish ols. A tentative diagnosis of oxytetracycline resistant phylococcal enterocolitis was supported when examination a rectal smear showed complete predominance of clumps gram positive cocci The oxytetracycline was immediately placed by oral erythromycin (400 mg six hourly) and gurt was given The patient was given a pint of blood lowed by other intravenous fluids but he died at 1 00 A.M. Nov 6.

### *cropsy Findings*

On opening the abdomen there was evidence of a healing ritonitis. Several loops of bowel were adherent in the region the cæcum but no free pus was present The whole pearance was no worse than that usually found after tra abdominal manipulation.

A striking feature was the presence of numerous enlarged ft lymph nodes in the mesentery of both large and small owel. The mucosa of the lower jejunum and ileum was utely congested and in the last 2 inches of the ileum enlarged mph follicles were again a striking feature. The mucosa of e large bowel was congested in its upper $1/_2$ in. The bowel ntents were liquid and dark green in colour

Greenish pus was found in both main bronchi both lungs ere oedematous and in their lower halves showed tiny areas f bronchopneumonic consolidation The spleen did not pear unduly abnormal There was no trace of kidney eter or renal artery on the right side the left kidney was larged but of normal appearance No significant abnor ality was found in any of the other organs.

Histological examination of the small bowel showed an ute inflammation of non specific type

### *cteriology*

Pus taken from the abdominal cavity at the second opera on showed a scanty growth of *Escherichia coli* sensitive to loramphenicol, chlortetracycline and oxytetracycline but nsitive to streptomycin.

On Nov 5 four days after commencing oxytetracycline rapy the stools showed numerous pus cells and gram sitive cocci mainly in clusters with a few gram negative cilli. This was taken to be presumptive of staphylococcal terutis and the organism indeed proved to be a coagulase sitive *Staphylococcus aureus* Using the disc method was proved to be insensitive to penicillin 0·5 µg chlor racycline 10 µg, oxytetracycline 10 µg Sulphatriad µg, and streptomycin 20 µg slightly sensitive to erythro ycin (10 µg.); and sensitive to chloramphenicol (40 µg) Blood-culture and throat swab taken the same day grew an identical organism The urine grew only scanty nterococci.

At necropsy cultures were taken from intestinal contents, mesenteric lymph nodes, lungs and spleen and each produced a *Staph. aureus.*

In all these investigations none of the usual bowel or mouth organisms was obtained pure cultures of *Staph aureus* being grown. These organisms all had similar antibiotic sensitivities Using the tube dilution method they were insensitive to oxytetracycline up to a strength of 1250 µg per ml; sensitive to erythromycin 0·3125 µg chloramphenicol 0·25 µg strepto mycin 12 5 µg and penicillin 25 µg The organisms from the throat (ante mortem) and from the lung and fæces (post mortem) were of the same phage-type (53/75+)

## Comment

The infecting organism seems to have been the *Staphylococcus pyogenes* present in the patient's anterior nares, which after administration of oxytetracycline rapidly became resistant to that drug The intra peritoneal abscess found at the second operation con tained only coliform bacilli on culture moreover the staphylococcus isolated after death from the bowel and from the lungs was of the same phage-type as that present in the nasopharynx during life.

Hay and MacKenzie (1954) found that in five cases in which phage typing was done three different organisms were respon sible As a further check against the possibility that cross infection by a drug resistant organism was the source of the infection all those who had been in contact with two of their cases were swabbed and none were found to carry resistant organisms

In our case the symptoms appeared on the fourth day of oxytetracycline therapy and by this time the responsible staphylococci were fully insensitive to the drug *In most reported cases the onset has been equally* early and it would appear that drug resistance, if it is going to develop develops quickly Oxytetracycline has been given for long periods—in some cases for many months—without adverse effect on the intestinal flora or the development of drug resistance

In the treatment of staphylococcal enteritis erythro mycin is the drug of choice and staphylococcal antitoxin can reasonably be given to combat the intense toxæmia Supportive measures include the restoration and main tenance of fluid and electrolyte balance, and intravenous fluids infused at the rate of 1000 ml per hour may be required (*Lancet* 1954) Yogurt was given in this case in an endeavour to repopulate the bowel with a non pathogenic organism which would compete with the staphylococcus There is clinical evidence of its value (Polymenakos 1954) but this needs confirmation

As already stated, we think it probable that our patient entered the hospital as a nasal carrier of the organism We suggest therefore that, wherever possible nasal swabs should be taken from patients who are about to undergo a major operation—especially if an indwelling stomach tube passed through the nose is likely to be used after the operation Gould and Allan (1954) have reported encouraging results in the treatment of nasal carriers using oxytetracycline cream In none of their cases did resistance to the oxytetracycline develop, but we feel that the routine use of this drug might be dangerous

## Summary

Fatal drug resistant staphylococcal enterocolitis fol lowed oxytetracycline (terramycin) therapy in a patient recovering from appendicitis and peritonitis. Less than 4·0 g of oxytetracycline had been given when the symptoms first appeared and despite the use of erythro mycin and supportive therapy he died about twenty four hours later A staphylococcus resistant to penicillin, *chlortetracycline* and oxytetracycline was *isolated from* the throat bowel, and blood, and from the viscera after death

In treatment erythromycin and staphylococcal anti toxin should be given with supportive measures. This complication could perhaps be prevented by preopera tive treatment of nasal carriers by topical application of an antibiotic

We are indebted to Prof W Arthur Mackey and Dr J C J Ives for their help and advice in the care of this case and to Dr P Pullar for the necropsy findings We wish to thank Dr R E O Williams, of the Staphylococcal Reference Laboratory Colindale for the phage typing also Dr R K Phillips medical director of Pfizer Ltd for his interest

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# VIRILISM DUE TO OVARIAN ARRHENOBLASTOMA

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The term arrhenoblastoma was first used by Meyer (1925) to describe an ovarian tumour originating from vestigial testicular tissue He observed that the more differentiated histologically was the tumour the less pronounced was the virilising effect

Most workers subdivide arrhenoblastomata into three types the highly differentiated mature type (testicular adenoma of Pick), the intermediate or mixed type, and the undifferentiated or sarcoma like type Recurrence is rare in the first but commoner in the third variety The tumours are small or moderate in size but occasionally may be as large as a man's head They usually cause symptoms during the reproductive period, and one case at least has been seen as early as at the age of 15 (Novak 1952) Henderson (1951) reported the tumour in two sisters

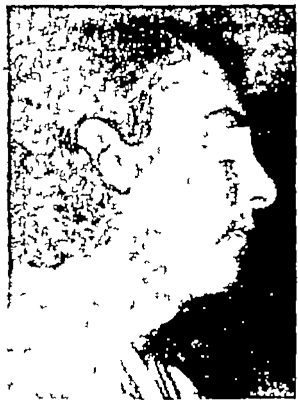

Fig 1—Patient aged 16, showing facial hirsuties (May 2, 1952)

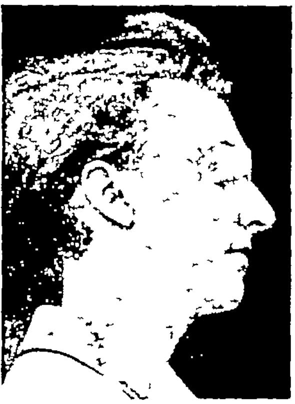

Fig 3—Patient in May, 1954 two years after removal of tumour

The incidence of malignancy in arrhenoblastoma is stated by Javert and Finn (1951) to be 22% They think that it is usually possible to decide whether a tumour is malignant or not on clinical grounds at laparotomy, and they advise radical surgery except in young women with apparently benign unilateral tumours

There is at present, among pathologists interested in this condition, no general agreement on the classification of virilising tumours of the ovary (arrhenoblastoma, lipoid cell tumour, ovarian hypernephroma, adrenal-like tumour, adrenal-rest tumour, masculinovoblastoma, luteoma, &c ) Thus Teilum (1946, 1952), Pedersen (1947), and Varangot (1952) classify these tumours as androblastomata and regard the various histological types as growing from a multipotential male mesenchyme cell which has the ability to differentiate in various directions Novak (1952) and Erez and Yenen (1952), however, regard masculinising luteomas, adrenal-like tumours, and ovarian hypernephromata as originating in adrenal rests within the ovary

There are many recent good descriptions of the clinical picture associated with arrhenoblastoma—e g , Forgeau and Gentin (1951), Thomas et al (1952), Novak (1952), Hughesdon and Fraser (1953), and Smiley et al (1953) Most workers emphasise that defeminisation takes place masculinisation follows later The decision whether a suprarenal or an ovarian tumour is responsible for masculinisation may, in the absence of a palpable mass, have to await laparotomy The urinary excretion of 17-ketosteroids may be increased or normal in cases of arrhenoblastoma If the excretion is increased preoperatively, one will expect a fall after removal of the tumour , postoperatively repeated estimations may be of some value because an increase in excretion later will suggest recurrence or metastases

## Case-report

The following case is typical of arrhenoblastoma (intermediate type) developing at an early age.

A schoolgirl, aged 15, was first seen in November, 1951, when she complained that six months previously her singing voice began to break, and later her speaking voice became low pitched Three months before being seen she noticed increasing hairiness of the legs and two months later hairiness in the beard area For six months there had been complete amenorrhœa, before which her periods had been scanty for six months, coming regularly every two weeks The menarche had been at the age of 13 and the menstrual periods had been normal for a year She had always been tall for her age, but in the previous year she had grown $1^1/_2$ inches

*Previous Diseases* —None of note except psoriasis for many years

*On examination* she was intelligent, 5 ft 8 in tall, and 8 st $13^1/_2$ lb in weight She was obviously worried about the physical changes taking place in her Her voice was deep and there was slight hairiness of her upper lip, chin, and cheeks Pubic hair was of male distribution, and her legs were very hairy Her thyroid gland was slightly enlarged and her breasts were small, with a moderate amount of hair round the areolæ Her external genitalia were normal. Her general configuration was of the male type, with a prominent Adam's apple Psoriasis was present on the trunk

*Investigations* —She was apyrexial , her urine was normal on routine examination , and an intravenous pyelogram and a glucose tolerance test for five hours were normal The urinary excretion of 17 ketosteroids was 9 mg in twenty-four hours (within normal limits) Rectal examination of the pelvis did not reveal any abnormality

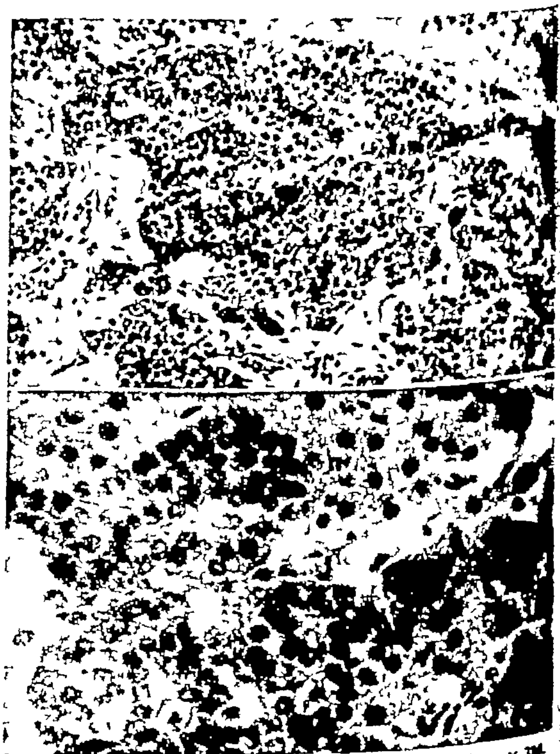

Fig 2—Ovarian arrhenoblastoma : above × 130 ; below × 3

*dpatient Observation*—In April 1952 she weighed 3½ lb., and the hairiness of her chin had much increased 1)

*readmission* vaginal examination under general anæs a revealed a soft cystic swelling in the left uterine adnexa uterus was small and anteverted the right adnexa felt al, the clitoris was slightly hypertrophied and the were normal The urinary excretion of 17 ketosteroids again within normal limits (7 8 mg in twenty four hours)

*parotomy* early in May 1952 showed the left ovary cystic and rather smaller than a tennis ball. The right y and the uterus appeared normal, and palpation of both arenal glands revealed no abnormality The left ovary removed and sent to Prof R W Scarff who reported ollows: A smooth whitish ovoid tumour 2½ × 1½ in. On section this proved to be a unilocular , its wall in many places almost paper thin but here and thickened up to ¼ in. by pale brownish yellow tissue in the fibrous capsule The inner aspect was uneven thin fibrous strands stretching across the cavity in es. Numerous blood vessels could be seen in the cyst . Section showed a fibrous cyst wall within which there a layer of tumour tissue bounded internally by flattened helial cells. The growth was composed of columns and ps of epithelial cells with large darkly staining nuclei relatively little cytoplasm, in some areas showing attempts ubule formation In between the columns and tubules were groups of larger cells with more abundant eosino- ic cytoplasm, strikingly resembling the interstitial dig cells of the testis. The appearances were those of an enoblastoma of the ovary At one end of the specimen e was recognisable ovarian tissue in which there were small cular cysts, and a portion of fallopian tube (See fig 2)

*ostoperatively* regular menstrual periods lasting four days arted after exactly a month. In August 1952 the patient s and legs were less hairy and her breasts were filling out April, 1953 there was no hairiness of her face and legs, her general appearance and manner were more feminine psoriasis, however was worse. By April, 1954 she eared to be a normal female in every way (fig 3) although voice was still low pitched Her interests and pastimes those of a woman. Pelvic examination was normal amination in October 1954 showed no change The nary excretion of 17 ketosteroids was still normal

## Comments

In spite of her youth at the time of diagnosis this tient presented the typical features of defeminisation d virilism due to an ovarian arrhenoblastoma It is ended to keep her under periodic observation when urinary excretion of 17 ketosteroids will be estimated cause this may in spite of normal preoperative dings, help to detect any recurrence.

Most textbooks describe ovarian arrhenoblastoma as ry rare but in a non-exhaustive search of the literature ce 1946 twenty four published cases have been found

## Summary

A typical example of an ovarian arrhenoblastoma ntermediate type) is described in a girl aged 15

Our thanks go to Professor Scarff for the histological port and to Mr T Crossley for the photomicrographs.

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# TETANUS TREATED WITH INTRAVENOUS MEPHENESIN

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JUDGING by the case recorded below, mephenesin can be very useful in the treatment of tetanus As a muscle relaxant this drug acts centrally by diminishing the reflex excitability of the spinal cord and not on the myo neural junction like curare It does not act on the higher centres and therefore does not affect conscious ness Above all it does not inhibit respiration

On Oct 26 1954 a muscular youth, aged 16 was admitted to the Reedyford Memorial Hospital Nelson, with tetanus. Seven days earlier he had cut his thumb with a knife in a cow shed and treated the wound himself Five days after he had wounded his thumb he noticed discomfort in his jaw on eating his dinner Next morning his jaw and neck felt stiff He consulted his doctor and was sent to hospital as a suspected case of tetanus.

*On examination* he had a characteristic risus sardonicus and a fair amount of trismus (he could open his mouth only half an inch) He had severe neck rigidity some opisthotonos, and severe pain in his back muscles On his left thumb was a dirty looking scab about an inch long

*Treatment and Progress*—On admission he was given mephenesin 1 g and antitetanic serum 100 000 units intra venously He was heavily sedated and given penicillin 500 000 units six hourly Intravenous mephenesin 1 g controlled his spasms for only about two hours consequently within the first ten hours in hospital it was necessary to give five such injections We then decided to set up an intravenous isotonic infusion of 4 5% dextrose and 0 18% sodium chloride con taining mephenesin 4 g per litre to maintain a constant blood mephenesin level and to be able to increase or decrease it at will by adjusting the rate of the drip flow We added 5000 units of heparin to each litre bottle To control the spasms a litre of this solution was used every six hours. After thirty-six hours we increased the strength of mephenesin in the dextrose-saline solution to 6 g per litre and gave about 3 litres of this solution every twenty four hours. This rate was main tained for ten days, the drip sometimes being run as slow as 25 drops per min. when no spasms were occurring and some times as fast as 160 drops per min. when the spasms were severe

At no time was there any depression of respiration or any sign of hæmoglobinuria. After ten days the spasms diminished in intensity and frequency and the amount of mephenesin required to control them fell proportionately The dripper was discontinued after two weeks when 198 g of mephenesin had been given. The patient made an uneventful recovery and was discharged just three weeks from the day of admission.

The hæmoglobinuria that is sometimes caused by intravenous mephenesin is probably due to the fact that the osmotic pressure of a 10% solution of mephenesin is at least six times that of an isotonic solution Thus multiple injections of a 10% solution directly into the blood stream will very likely cause hæmoglobinuria The reason why we were able to give 198 g of mephenesin in two weeks without causing hæmoglobinuria was probably that we gave it in isotonic dextrose saline solution thereby reducing its osmotic pressure to a level at which it has no effect on the red cells

The treatment of this severe case of tetanus, in which the first signs appeared less than five days after the initial infection resolved itself into a matter of sedation anti biotics, and an intravenous infusion of mephenesin in isotonic dextrose saline solution of which up to 18 g was given in twenty four hours and maintained for at least two weeks without ill effect

I am grateful to Mr D A. Richmond and Dr J Shafar under whose care this patient was treated for permission to publish and to Mr Lloyd Hagan Chief Pharmacist at the Hospital for his advice and help in all phases of the treatment of this case

# Reviews of Books

## Die Brucellose als Anthropo-Zoonose

*Febris Undulans* W LÖFFLER and D L MORONI of the University Medical Clinic, Zürich, W FREI, formerly of the Veterinary Pathological Institute of the University Berlin Springer 1955 Pp 193 DM 29 60

DESPITE the voluminous literature on brucellosis, few if any textbooks are comprehensive, and this book makes no claim to fill the gap But by joining forces to coördinate and expand two earlier publications on the disease in man and in animals, the authors have covered a very wide field This valuable coöperative effort by the medical clinic and the veterinary bacteriological institute of the University of Zürich was inspired by an investigation of the " incomplete antibodies " giving rise to the blocking phenomenon for which the Coombs test was designed, and by the alarmingly high infection with brucella of Zürich's milk-supply Brucella infection of the udder was found to be thirty times as common as tuberculous infection in the herds The authors also felt that the time had come to review the effect of antibiotics on therapy of human and animal infection

The title, by putting human brucellosis in the same class as animal zoonoses, tends to obscure the fact that brucella is the outstanding example of the group of infections of which animals are the sole reservoir, and the authors only hint at the difficulty of eradicating the animal, and consequently the human disease This difficulty is greatest in backward countries where goats are the chief reservoir of infection ; but even in countries such as the United States and the United Kingdom the sharp reduction of bovine disease has revealed a hard core which is still causing a considerable number of human infections It is, therefore, curious that the authors have not described more fully the disease in wild animals, for this may account for some of the mysterious reinfections of herds of cattle despite elaborate precautions Rather more than a page is given to avian infection, but the part which birds may play in the mechanical spread of infection is not mentioned On the other hand, such difficult problems as agglutination-blocking and the significance of skin allergy are handled with great skill and judgment

## Leg Ulcers

*Their Causes and Treatment* S T ANNING, T D , M A , M D Camb , M R C.P , assistant physician, dermatological department, the General Infirmary, Leeds London J & A Churchill 1954 Pp 178 18*s*

IN this small, readable monograph Dr Anning has successfully reviewed and integrated the extensive literature on this subject, and he gives 20 pages of references The survey of his own work includes an excellent section on non-surgical methods of management As a dermatologist Anning gives little space to surgical methods, and this may mislead the reader into thinking that surgery has no place in treatment He emphasises the relation of most ulcers of the leg—even those associated with obvious varicose veins—to previous deep thrombosis This view, which is rapidly gaining ground, is in full accord with all modern work on the subject The chapters on ætiology and differential diagnosis are good He writes agreeably and approaches every aspect from its historical angle—which makes for interesting and sometimes amusing reading

## Maladies des os et des articulations

STANISLAS DE SÈZE, professeur agrégé à la Faculté de Médecine de Paris, ANTOINE RYCKEWAERT, médecin assistant des Hôpitaux de Paris Paris Flammarion. 1954 Pp 1240 Fr 9300

THIS massive tome is one of the seventeen volumes on every branch of medicine so far published by this firm with many more still to come

It is in loose leaf form and can be brought up to date by annual additions The necessary metal work contributes to its weight, and at 8¼ lb it is no bedside book it demands indeed, an armchair and lectern But it is written in straight-forward style easily read by those with only a fair knowledge of French. The lay out is clear, and the illustrations, particu-larly radiographs, are well produced , but the index is far too short to be of any real use It naturally expresses the French approach to orthopædic problems, and—a criticism which applies equally often to British and American works—the references are patriotic rather than world wide Treat-ment is described relatively briefly many possibilities are offered, but the writer's preference is not sufficiently indicated

The book is rather too long for the average student, but with suitable annual additions may, in France, take the place of the " Year Books " from Chicago which are so useful to the English-speaking world

## Lecture Notes on the Use of the Microscope

R BARER, M C , M B , B.SC , demonstrator in anatomy, University of Oxford Oxford Blackwell Scientific Publications 1953 Pp 76 6*s*

MEDICAL students are seldom taught the principles of microscopy in any detail, and often come to use their microscopes as many drivers use their cars—without much understanding of the works This little book not only explains how a microscope should be used, but also gives a short account of the optical principles on which it is designed, and of the structure and purpose, as well as the care and management, of the various parts A student beginning microscopical work should be g to read quickly through it, and to have it to refer to he gets into difficulties

## Développement psycho-moteur du premier âge

Dr CYRILLE KOUPERNIK Paris Presses Universitai de France 1954 Pp 197 Fr 500

André Thomas and his collaborators have made compre-hensive neurological studies of the developing infant Dr Koupernik's little book is a kind of handy guide to such major works Though he seems to have writte it hurriedly—there are misprints and some ill founded assertions—he has done a service by drawing attention to the neural significance of phases of physical develop-ment and by pressing the point that central nervo disorders in infants can and should be diagnosed early

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**Atlas of Congenital Cardiac Disease** (New York American Heart Association 1954 Pp 62)—It is nearly twenty years since Maude Abbott's *Atlas* was first published and for some years it has been unobtainable despite m requests for its republication Now, thanks to the American Heart Association, a splendidly produced reprint has appe This work has long been regarded as a standard classic, apart from James Brown's book, nothing comprehensive the subject was published until Dr Helen Taussig's mono-graph, which had the advantages of adding surgical experi to clinical and necropsy observations But even the adv of more accurate assessment and operative findings does not detract from the value of the *Atlas* In this each page of illus-trations faces a descriptive text, which contains valuable references and histological data The first part deals with embryology and comparative anatomy, while the second is a clinical classification divided into acyanotic and cyanotic groups There is also a chart analysing the 1000 cases on which the *Atlas* was based

**Isaac and Œdipus** (London Routledge & Kegan Paul 1954 Pp 131 15*s*)—In this scholarly book the late Dr Erich Wellisch put forward his view that the theme of the binding and symbolic sacrifice of Isaac, the only begotten and dearly loved son, by his father, Abraham, represents a spiritually and culturally higher solution of the central parent child conflicts than the Œdipus complex Wellisch first saw the father son conflict in three historical stages first, the primitive society where rivalry between father and son led often to infanticide , then the compromise, tragic and unstable, of the Greek philosophy, which sees man as the hapless plaything of the gods, yet guilty for his own crimes, then the biblical solution, paving the way for a loftier concept both of parent-child relationships and of the nature of God. The theological commentaries, iconography, and legends connected with the Akedah are well set out

THE LANCET

*LONDON SATURDAY FEB 26, 1955*

## Enough Doctors?

As reported in our Parliamentary columns the inister of Health announced last Monday that has appointed a committee to inquire into e number of doctors needed for the future In nsidering this question three and a half years ago [1] tentatively concluded that the number of doctors ualifying annually in England and Wales was about 00 in excess of the number of permanent posts vailable in the National Health Service (as consultants or principals and partners) and in the other rvices, while in addition there was a yearly surplus some 300 from Scotland Since that time the ritish Medical Association has expressed growing -and very proper—anxiety about the possible effects such a surplus continuing and Ministerial action as expected sooner But the delay has the advantage hat the committee will have more solid evidence on hich to work. When we made our own estimate he N.H.S was in its early stage, but it has since xpanded considerably, and a clearer picture of its rmanent structure can now be formed The figures ppearing on p 440 show a rise in the total of consultants in Great Britain from 6470 in 1951 to 7136 y the middle of 1954 and during the same period any new practices have been formed in underdoctored areas and many assistants have been made artners or principals Even so, the prospects of a doctor becoming a consultant between the ages of and 40 or a principal or partner in general practice between 30 and 35, are still not as good as they should be The expansion of consultant posts has somewhat exceeded what was forecast but the number of new consultants has not increased correspondingly, ince some of the new posts have been filled by men already established The figure given for senior registrars in specialist training (943) is approximately related to the expected needs of future replacement and expansion but it probably does not include a number holding academic appointments and it specifically excludes 363 'others many of whom are in what are euphemistically described as 'transitional posts,' after completing their training and are trying to obtain consultant or equivalent appointments The plain fact is that there are still far too many applicants for consultant posts, and that entry into general practice is too difficult—though it would perhaps become easier if young doctors were more willing to follow the Minister's advice to go North In contrast to the abundance of senior registrars, there is a continued shortage of junior hospital staff especially registrars.

The present situation reflects the uncertainties of a developing service, aggravated by the post war popularity of medicine as a career and it may well need special remedies The committee's main task, however, will be to look ahead Since 1947 some 3000 doctors a year have been added to the Medical Register There was a remarkable fall to 2320 in 1953 but this was partly artificial, because many had registered early (in 1952) to avoid provisional registration The numbers of students reported as beginning the study of medicine in Great Britain and Ireland have declined steadily from 2725 in 1949–50 to 2280 in 1953–54 but this reduction will not have its full effect on qualification until 1957 The total of 7000 odd consultants has now reached the figure mentioned by the Ministry of Health in its original memorandum on consultant and specialist services, but it falls short of the optimum particularly in some of the specialties The number of doctors who will be required in general practice for expansion and for replacement, is again not easy to predict—especially as we must remember that the traditional, and persisting, pattern of practice was determined as much by the economic prospects for the doctor as by the needs of the population. The number of new practices required to bring under doctored areas up to the average level can be estimated with fair accuracy, but there is still no retiring age by which to calculate the needs of replacement The terms of the Danckwerts award may eventually enable general practitioners to retire earlier

To see further ahead is naturally even harder The present establishment of the N H.S is necessarily a compromise between the needs of the community and the amount of money it is prepared to spend on health We can do no more than guess at the ideal future ratio of doctors to the population Some of the work which they do now may one day be delegated to ancillaries [2], but, on the other hand, if their energies were not so fully occupied with curative medicine, they could devote more of their time to advising their patients in the broader aspects of health Maternity and child guidance centres have shown what can be done in a limited field, and experience gained from new housing estates may considerably widen our concept of the family doctor A real effort to practise more preventive medicine would help to reverse the tendency to centre medicine on the hospital

Though it will obviously be impossible for the new committee to answer all the questions which arise we hope it will be able to consider some of them The immediate task is to survey the numbers of doctors needed by the N H.S and the other services as they exist today As regards the supply of doctors to the profession it is clear that—though medical schools have so far found little difficulty in maintaining either the quantity or the quality of their entry—the demand for medical training has slackened a little The slackening is due partly to an expected reaction from the post war enthusiasm and perhaps to greater success on the part of schoolmasters in discouraging unsuitable candidates, but one reason for it, undoubtedly, is anxiety about the prospects of a medical career Clearly, if we are to maintain our standards—let alone raise them—would-be students must be confident that places in the medical schools are related to opportunities of employment after qualification The committee will perform a most valuable service if it can give a realistic and fairly precise estimate of present needs as well as indicating the kind of future developments that may make periodic revision necessary

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[1] *Lancet* 1951 ii 331; *Ibid* 1953 i 779

[2] *Ibid* 1953 i 29

## Cytotoxic Agents in Malignant Disease

THE value of cytotoxic agents, especially the nitrogen mustards and similar mitotic poisons, in the treatment and control of the reticuloses and chronic leukæmias is now well known[1], and a protracted study of one of these substances, 'Myleran,' in chronic myeloid leukæmia is described on an earlier page of this issue by Dr GALTON and Dr TILL The success of these drugs has very naturally led to their trial in malignant diseases of the hæmopoietic system (including lymphosarcoma and reticulosarcoma) and of other systems Unfortunately the results have not been very encouraging

In 1951 PATERSON and BOLAND[2] reported that tretamine (triethylene melamine, T E M) had no effect in 3 cases of carcinoma of various types WRIGHT et al[3] found that tretamine had no detectable effect in 12 patients with carcinomas, 4 patients with fibrosarcoma seemed to improve, but 6 with other types of sarcoma were unaffected Only in some cases of bronchial carcinoma have results been unequivocally favourable LENTI and GAVOSTO[4] gave tretamine to 10 patients with this type of carcinoma and noted temporary symptomatic and radiographic improvement in 2 RAPHAEL and REILLY[5] used the standard nitrogen mustards to try to alleviate the effects of inoperable bronchial carcinoma, of 56 patients treated, 15 were judged to have gained significant palliation, which was especially noticeable in those with symptoms from obstruction of the superior vena cava SALINE and BAUM[6] administered tretamine by mouth to 15 similar patients in doses of 5 mg daily for four days, followed by 2 5–5 mg at intervals varying from one to six weeks according to the clinical response and the effect on the blood They observed useful alleviation of signs and symptoms in 4 patients, in each of whom there was evidence that the superior vena cava was obstructed All the patients died eventually, but their comfort in the survival period was notably enhanced SALINE and BAUM found 3 instances of the toxic effect of tretamine on the blood-forming tissues, and in 1 patient cortisone was given before the aplastic anæmia remitted

In frank malignant disease of the hæmopoietic system mustards are less effective than in relatively benign conditions such as chronic leukæmia and Hodgkin's disease MEYER et al,[7] reviewing the effect of tretamine on diseases of the lymphat system, classed lymphosarcoma among the les responsive lesions, and chronic lymphatic leukæm among the most responsive WINTROBE et al.[8] he that tretamine was of little value in lymphosarcoma reticulosarcoma, and pointed out that some patien with these diseases developed serious hæmopoiet depression when treated with this drug BLACKBU and KING[9] had no success from administration tretamine to 4 patients with reticulosarcoma

These results are disappointing It seems to hardly worth exposing patients to the discomfo and risks of cytotoxic chemotherapy for so uncerta a benefit Intravenous mustard is liable to ind vomiting, which is especially undesirable in patien with bronchogenic carcinoma and obstruction of t superior vena cava, who seem to be the only gro who are benefited at all consistently In such ca tretamine, which is less liable to cause vomitin may be given orally But tretamine has its own of disadvantages, including extreme variation in t effective dose between one patient and anoth and considerable risk of irreversible aplastic anæmi It is not surprising that tretamine has not b generally issued for the use of practitioners in t country—restraint for which we should be grate to the manufacturers The effectiveness of t cytotoxic agents in chronic leukæmias, Hodgkin disease, and some of the other reticuloses is n established These conditions are not usually classif as "malignant," though they sometimes termin in a malignant phase In the truly malignant disea radiotherapy clearly continues to hold the field alleviation, palliation, or even cure—judging by t results after five years When radiotherapy fail malignant disease, chemotherapy still cannot take ov

## Protecting the Motorist

THE motor-car that is badly driven or mechanica at fault is a grave menace to pedestrians and cycl But, as we all know, the motorist himself is a exposed to substantial hazard, and study of inju to drivers and passengers may suggest methods prevention A large proportion of such injuries seem be due to unexpected sudden loss of speed (Colonel R FORBES, of the Royal Society for the Prevention Accidents, has pointed out[10] that when a car crash after being pursued the occupants not uncommon leap out uninjured, and such relative immunity, suggests, may be due to the driver and passenger holding themselves ready for a collision) This impre sion is strengthened by LIVINGSTONE's[11] analysis some 3000 non-fatal injuries to motorists LIVINGSTON found that about two-thirds of the injuries were apparently due to impact or crushing and one third to "whiplash" strain, wrenching, or protective rotation Whiplash strain of the neck is due to momentum carrying the head forward on the trunk (or backward if the car is struck from behind) The driver is more liable than passengers to injuries of the t because of the steering wheel, but this protects somewhat from injuries to legs and pelvis, which ommoner among passengers Rather surprisingly **NOSTONE** found that the side of the car was almost sual a source of injury as the structures on the t of the interior—a finding which may reflect the ent-day preference for the wide saloon without unning boards which give strength and protection his series there was but 1 case of burns—from hted cigar—and indeed it is now very rarely that r bursts into flames after a crash The series uded only 3 cases of cuts from flying glass—sure ence of the benefits of safety glass, which is now d almost universally, although in this country the demands only that it be used for windows facing and aft. Safety glass is of two main types—inated and toughened

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[1] *Lancet* 1954, i 1118

[2] Paterson E. Boland J *Brit J Cancer* 1951 5, 28

[3] Wright, J C Prigot A, Wright, L T, Arons I *Arch intern Med* 1952 89, 387

[4] Lenti G Gavosto, F *Minerva med, Torino* 1953 44, 1

[5] Raphael M. Reilly, C N *Dis Chest* 1954 25 215

[6] Sal[illegible] Baum, G L *J Amer med Ass* 1954 156 1493

[7] Meyer, L M Schwartz S O Sawitsky, A Beyers M F, Ritz N D Brahin C, Diefenbach W, Kleinschmidt, W, Friedman I *Acta med scand* 1952 144, suppl 272

[8] Wintrobe, M M., Cartwright, G E Fessas, P., Haut A Altman S *Ann intern Med* 1954, 41, 447

[9] Blackburn E K, King, G M *J Fac Radiol., Lond* 194 6 96

[10] Personal communication

[11] Livingstone, R G *Surgery* 1954 36 1059

*minated glass* which comprises two sheets of glass a plastic interlayer was introduced into this country 912 and is still used for windshields in North America, re its fracture occasionally causes wounds and udons.

*oughened glass* introduced in 1933, is made by heating sheet of glass to near softening point and rapid enching" by blowing cold air on the surfaces the t is to produce compression on the surfaces and in llibrium with that, tension inside the glass Such s is now used in 90% of cars for the home market , according to the British Standards Institution ce 1933 not one single accident has been reported hich serious injury has resulted from sudden disintegtion of the glass.'[12] One criterion in standardising glass is the size of particles on fracture Here two flicting factors have to be considered: on the one d, the larger the particles the less will visibility be aired; on the other the smaller the particles the less be the risk of injury After exhaustive tests a revised tish Standard[13] last year laid down that the glass uld break into not less than 20 particles per sq in., pared with not less than 40 in the previous standard

What further precautions might prevent injuries? rease in the strength of the body would involve reased weight, and thus a more powerful and economical engine and stouter pillars might mselves be a source of accidents by limiting the er's vision. Projections inside the car should be ew as possible Outside door handles and hinges usually recessed but within, projecting window dles persist When recently a famous maker duced a model with balanced windows which could raised and lowered by hand and held in place by mple looking device on the door panel there were plaints from purchasers who apparently thought t they were not getting value for money, and e usual winding handle had to be restored The r seats could be fitted to face backwards, as in planes, without much trouble but the back of e body would have to be redesigned to allow quate vision to the exterior and it is very doubtful ther the public would take kindly to this rather ociable arrangement Upward extension of the ks of seats, to provide a rigid head rest should vent whip-lash injuries in collisions from the rear, t would be useless in the more common head on lision unless the head were held in place by a head band—a device that motorists would hardly d one A safety belt such as that used in aeroplanes ht be slightly more acceptable This would have be attached to the floor of the car or for the rear seats to a cross-member Undoubtedly such a belt would prevent many injuries to the pelvis and legs, and for protection against injuries of the back (and, in the case of the driver to the chest) it should extend upwards over the thorax, like a corset But those who travel by air know with what relief they undo the belt if it has been pulled fairly tight—as it should be—and it is questionable whether the motorist would wear it for long, at least in summer or would bother to attach it for short journeys But at least seats could be securely anchored, at present many are not A collapsible steering column would prevent crushing wounds of the driver's chest, but when the driver treads on the brakes in an emergency he presses very heavily with his hands on the steering wheel, and if this gave way braking might be dangerously impaired the critical strain would necessarily have to be so great that the driver's chest would still be in peril Again, the dashboard could be made of some material that would be rigid enough to support instruments and pockets but in collisions would make a less severe impact on the passenger's knees or face The occupant of the place beside the driver is more liable than anyone else in the car to leg injuries, and in the U S.A this place is known as the suicide seat Some American cars include a "crash pad"—usually a thick roll of sponge-rubber—running along the upper edge of the dashboard Such a pad should be particularly helpful for children but sponge-rubber may not be the material of choice **WHITE**,[14] in a striking indictment of the design of American cars insists that because of its quick recoil, sponge-rubber should not be used instead he recommends a light metal or other material that will fracture or yield on impact Sometimes the effects of an accident are made worse by passengers being flung out when doors fly open Attention should be given to designing doors that will remain shut in an accident and yet can be opened readily in an emergency and hinges should always be on the forward edge of the door

**GISSANE**[15] has remarked that 'the British motor car industry could perhaps gain considerable prestige by exploiting the design of a really safe car" But car manufacturers—like the makers of shoes and other commodities marketed competitively—are much concerned with what the public are prepared to buy Purchasers of cars may be reluctant to pay for safety devices unless these are conclusively and repeatedly shown to be of value Crash helmets have for almost fifteen years been widely known to be an indispensable safeguard for the motor cyclist yet it is only in the past three or four years that they have been much worn Lately at least one insurance broker has reduced by almost half the premium for personal accident insurance of motor cyclists who wear an approved crash helmet Motorists might be more willing to pay a little extra for safety devices if in return their premiums were reduced Unfortunately the statistics which have justified the reduction in the case of motor cyclists are lacking in regard to motorists partly because the value of any single physical safeguard is much less readily established and partly because, alone or in combination, such safeguards have not been fully tested

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[12] British Standards Institution CT(OC)3165 May 13 1954

[13] B.S. 857/1954 *Safety Glass for Land Transport*

[14] White A J The Truth about American Cars Published by Motor Vehicle Research Inc So Lee New Hampshire U.S.A 1953 Pp 48 81

[15] Gissane W *Practitioner* 1954 172 620

# Annotations

## CYCLOSERINE

ANOTHER antibiotic derived from the streptomyces group of fungi has been discovered The first accounts of it—not yet published—were given at a Veterans Administration conference at Atlanta on Feb 9[1,2] Cycloserine is said to be a broad-spectrum antibiotic active against tubercle bacilli, it can be administered by mouth, and preliminary clinical reports from the Metropolitan Hospital, New York, are sufficiently promising to have justified the Veterans Administration starting a large trial immediately So far there is no information about toxicity or bacterial resistance

Experience in the past ten years with antibacterial drugs in tuberculosis has shown what a large amount of laboratory and clinical investigation is needed before the value of a drug can be even roughly assessed But such experience has also led to the evolution of efficient organisations for cooperative research, and the speed with which they can produce practically valuable facts was well demonstrated by the Medical Research Council's early investigation of isoniazid three years ago[3] Cycloserine is said to be difficult to manufacture, and it is not yet being produced commercially either in this country or in the U S A , but, if further clinical trials prove it to be valuable, it will be marketed under the trade name 'Seromycin'

## THE PSYCHIATRIC DAY-HOSPITAL

THE idea of the day hospital for treating patients with nervous and mental disorders without increasing the demand on hospital beds was conceived independently by Bierer in this country and by Cameron in Montreal, and many psychiatrists are now interested, as was clear from a meeting at the Marlborough Day Hospital, London, on Feb 15 This meeting was opened by Dr Aron, who has himself been instrumental in setting up a day-hospital in Bristol[4]

Some mental hospitals allow outpatients to attend daily for psychotherapy and occupational therapy, but several speakers suggested that this hardly constitutes a day-hospital, which is a self-contained community in which the therapy derives from the community itself It was generally agreed that the day hospital should be an independent institution, but close liaison with local mental hospitals (as in Bristol and Montreal) or with a general hospital was desirable The facilities at the Marlborough and the Bristol day-hospitals include individual and group psychotherapy, occupational therapy, social clubs, art therapy, and physical treatments such as electroshock and modified insulin In Cameron's[5] opinion certain types of patient are best treated initially in a mental hospital and then transferred to the day-hospital Bierer[6] listed fourteen categories of patients suitable for attendance at the day-hospital Cameron's list is roughly the same, but he also admits relatively advanced schizophrenics and manic depressives—even some with hallucinations or with suicidal ideas Dr E G W Cross (who is now in charge of the Bristol day hospital) said that some types of psychopaths and chronic inadequate neurotics have to be excluded, but he has found that many chronic women neurotics derive more help from the day-hospital than from the neurosis centre He claimed that the staffing was very economical, since only one psychiatrist (himself) carried out all the therapy and ran the clubs, with the aid of one social therapist on a half-day a week, one secretary on and a half days a week, a sister, a staff nurse, th ward orderlies, and a help Dr Aron remarked th excessive economy in staffing, especially of psychiatr should be avoided The patients needed much psy therapy and attention from psychiatrists if they were benefit from attendance The relative cost of the d hospital patient in London and Bristol, compared w that of the mental hospital inpatient, was estimated about a third—an estimate that agrees with Camer in Montreal

Some speakers emphasised the advantage of the hospital in dealing with the over-dependent type neurotic patient Dr Bierer claimed that the preserv of contact with the outside community and the re situation constituted one of the main therapeutic facto and Dr Cross considered that the day-hospital, with becoming a dumping-ground, could prevent the es into mental hospital of many patients Dr Donald B also was strongly of the opinion that day hospitals c replace 80% of the mental hospital accommodation, that it was very bad for most neurotics to stay m than a few weeks in a neurosis centre, for if they sta longer it was almost impossible to induce them to t up once more the ordinary responsibilities of h and work

## PROGNOSIS IN BRACHIAL-PLEXUS INJURIES

A YOUNG engineer finishes his work, mounts his m bicycle, and hurries home to spruce up for a date T has been a slight drizzle, he brakes hard to avoid a c and over he goes Thanks to the pioneer work of the Sir Hugh Cairns his helmet saves him from a serious b injury, and he is lucky to escape with no broken bo He just cannot use his right arm

There must be few days in the year without an in of this sort in the British Isles Attempts to repair plexus have been unrewarding, and even exploration been decried because it yields little information of v and some which may mislead Yet, although the surg is virtually helpless to speed recovery, he can ope to make the limb less of an encumbrance or even an as The great stumbling block has been the difficulty prognosis in complete lesions, and a patient may h to wait many months and receive countless mani tions from the physiotherapist before it is finally dec that no recovery will take place and reconstru surgery is required

Work by Bonney,[2] although aimed at determining exact site of the lesion in brachial plexus paralyses, throw much-needed light on prognosis He studied axon responses in 13 patients with complete trac injuries of the brachial plexus The response to intradermal injection of histamine was tested on t *radial and ulnar sides of the forearm* and hand In fingers the cold vasodilator response was measured the finger-tips by means of heat-flow discs of tellurium a copper A positive response in either of these t depends on the integrity of the cutaneous axons to t area tested In 9 of the 13 patients some positive respo was obtained—which strongly suggested that the sens loss in these areas was due to a preganglionic les leaving the postganglionic axon intact to subserve th response These observations were compared with th local lesion by thorough exploration of the plexu The correlation of positive axon response in the limb wit the finding of myelinated fibres in the appropriate root the plexus was remarkably close, and clearly pointed to preganglionic site of injury of the particular plexus roots In this small series useful recovery ensued in 2 of the cases where there was no axon response and thus a mo distal injury, but in only 1 of the 9 in which a positi

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[1] *New York Times*, Feb 10, 1955
[2] *Times*, Feb 11 1955
[3] Medical Research Council *Brit med J* 1952 ii 735
[4] Aron, K W *J ment Sci* 1953 99 504
[5] Cameron D E *Mod Hosp* 1947 69, no 3
[6] Bierer, J The Day Hospital London 1951

[1] Hendry, A. M. *J Bone Jt Surg* 1949, 31B, 42
[2] Bonney, G *Brain*, 1954, 77, 588

ponse was elicited and the lesion was likely to be n.

Further study is clearly necessary to confirm this first pression of a poorer prognosis with a lesion which is any rate partly, preganglionic and close to the cord nney's work clarifies two previously misleading find s in exploration of the plexus—a normal looking nus, and myelinated fibres in a funicular biopsy of ls or roots. Both are consistent with a severe and bably irreparable lesion above the posterior root glion and close to the cord Testing the axon responses cases such as this may avert an unwarrantably hopeful gnosis and rightly lead to prompt reconstructive gery

## FLAVONOIDS AND THE THYMUS

OME plants contain large amounts of flavone deriva s which often account for the yellow colours A onoid may be an essential food factor at least for the neapig; and "vitamin P" which Szent Györgyi racted from the skin of citrus fruits and paprika ms to be a mixture of flavone derivatives Hitherto se substances have not been isolated from animal ues

zent Györgyi, who in 1928 first isolated vitamin C m the adrenal gland, has now found a flavonoid pig nt in the thymus gland At a conference held in w York on the biochemistry of flavonoids he showed g of a yellow powder which he had extracted from re than 15 kg of calf thymus glands[1] In man the mus grows until the age of 2 and persists until puberty n it usually atrophies Its function has not been covered Reports that an extract delays the onset of t heat[2] and that phosphorylated hesperidin (a flavone ivative) diminishes fertility[3] may gain new signifi nce in the light of Szent Györgyi's discovery

## VITAMIN C AND INFECTIONS

VITAMIN C, in addition to influencing wound healing believed by many to combat infection The cause of s possible effect is obscure but ascorbic acid (vitamin in the presence of oxidising agents degrades many ysaccharides.[4-6] Polysaccharides in bacterial-cell walls ght therefore be attacked and the bactericidal effect a mixture of ascorbic acid and oxidising agent[7 8] ght be due to this action A further possible effect on mucin Despite its useful lubricating functions in body mucin may aid infective processes by protect g pathogenic micro-organisms from the attack of the ly defences and by enhancing their virulence[9 10] erefore ascorbic acid together with oxidising agents attacking local accumulations of mucin may promote sistance to infection and recovery from attacks by ngi, trypanosomes, bacteria and viruses

Treatment with ascorbic acid and percarbonate has en reported to result in rapid improvement in stoma tis, gingivitis and oral mycosis; and Ericsson[11] suggests at topical application to epithelium covered surfaces ay be helpful in many infections But since mucoids n the tissues might be attacked, it would seem advisable o exercise caution in applying this treatment to mucous embranes

## ARTIFICIAL FEEDING OF INFANTS

PÆDIATRICIANS have been telling us for a long time that in the artificial feeding of infants the quantity of the feed is just as important as its quality and many of them believe that the artificially fed infant is too often artificially *underfed*[1 2] Their opinion has lately been convincingly confirmed by Hytten and MacQueen[3] who using an ingeniously simple method, determined accur ately how much fluid, protein fat and carbohydrate were received by a series of 100 infants under three months of age all reared at home They found that 60% of the infants were receiving less than the generally accepted requirement of 50 calories per lb (120 calories per kg) per day and 40% were getting less than 100 calories Underfeeding to this degree is a serious matter; but its correction should not be difficult since about 75% of artificially fed infants receive the same type of food —namely National dried milk.

Of the causes of underfeeding the most important is the instructions given on or in the tin of dried milk. It is debatable whether such instructions should be given at all and in the U S A manufacturers advise parents to consult their doctor about details of feeding The instructions provided with a tin even if they were correct (which is seldom the case) could not possibly deal with the individual variations of particular infants Hytten and MacQueen point out that the instructions issued with National dried milk fulfil the infant's calorie requirements only if the measure is tightly packed with full-cream powder but mothers are not told this With part skimmed milk even tight packing cannot meet the calorie requirements The measure of sugar—usually expressed in teaspoonfuls—may also be very inaccurate The late Eric Pritchard had a collection of spoons all sold as teaspoons whose liquid capacities varied from 30 to 90 minims when measuring sugar the variation would be even greater If instructions are to be issued with National dried milk, they should be amended to recommend one level measure to 1 oz of water, with the addition of 1 drachm of sugar to each 4 oz of the mixture This would largely abolish underfeeding, and it would simplify matters for mothers who are not adept at working out the figures The rule is half the infant's weight in pounds is the volume in ounces of a four hourly feed and the number of level measures Occasionally this rule may lead to what is technically overfeeding, but we have been too much afraid of this in the past, and babies can take it more readily than is generally supposed However clear and accurate the instructions success in following them depends on the intelligence and resourcefulness of the mother The doctor's obligation is not ended when he has given verbal or written instructions

When artificial feeding first became practicable the importance of vitamins was not recognised so scurvy and rickets became very common Nowadays we do our best to see that every child has plenty of vitamins and it seems a slur on the medical supervision if there is even a mention of scurvy or rickets But it may be too readily assumed that the gap between the required amount and a toxic dose is very large and there has been little emphasis on control of dosage The question of vitamin D is the most disquieting Dried milks and evaporated milks contain additional vitamin D, cod liver oil is issued free to every mother—with persuasive propaganda to make sure it is given—and other foods such as cereals and glucose may contain added vitamin D Creery and Neill[4] have suggested that in our anxiety to avoid rickets we may be in danger of poisoning our children with vitamin D and Ball[5] believes that over dosage is relatively common Even without firm proof, these warnings must not be ignored A survey on the lines of that by Hytten and MacQueen might reveal just how much vitamin D infants really are getting, and if the intake is found greatly to exceed the requirements it should be reduced, for such excess can do no good and may be doing serious harm Whether vitamin D is best provided in milk, as Woodcock[6] suggests, or in cod-liver oil is debatable, but it should be contained in one or the other, not both Until we have more facts about vitamin-D intake it would be wise to assume that most babies in this country are getting more than they need, and to remember that cod liver oil is strong stuff

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## CEREBELLAR DEGENERATION

CONFUSION over the various forms of degeneration of the cerebellum and associated tracts in the spinal cord has been partly dispelled by Greenfield[7] There are two major pathological groups in one the long tracts in the spinal cord are chiefly affected, and in the other the cerebellum itself The best-known example of a predominantly spinal disorder is Friedreich's ataxia, in which the principal changes are in the dorsal columns and neighbouring parts of the lateral columns, with fairly complete degeneration of the direct, and slighter changes in the indirect, spinocerebellar tracts, there is usually some atrophy and sclerosis of Clarke's column and degeneration of the dorsal roots, especially in the lumbosacral segments In some affected families clinical and pathological variations from typical Friedreich's ataxia are found, and rarely, in an individual patient, the disorder may be combined with a more common familial disease—peroneal muscular atrophy The familial and usually non progressive condition described by Roussy and Levy[8] in 1926, of which the main features are pes cavus and absent tendon reflexes in the legs, sometimes combined with slight ataxia, some wasting of the distal leg-muscles and small muscles of the hands, and extensor plantar responses, is a further link between Friedreich's ataxia and peroneal muscular atrophy, and all three conditions have been described in different members of the same family[9]

In 1893 Marie[10] described familial cerebellar ataxia which developed slowly in adult life, and differentiated this from Friedreich's ataxia His report was based on four families previously described by others In some of these cases necropsy reports became available only after Marie's paper appeared, and in 1907 Gordon Holmes[11] pointed out that in the group described by Marie the lesions were not always the same In two of the families the degenerative changes were predominantly in the spinal cord, in one the cerebellar cortex was mainly affected, and in the fourth the microscopical examination was incomplete Greenfield has analysed all the reported cases of familial cerebellar degeneration with clinical onset in adult life in which there are satisfactory pathological reports, and he finds that they fall into two groups, in addition to the predominantly spinal cases In the first group, originally described by Menzel in 1891,[12] the degeneration affects principally the middle cerebellar peduncles, the pontine nuclei, the medullary olives, and the cerebellar white matter and cortex in that order of constancy This in fact is essentially a cerebello petal degeneration, and it is apparently the same disorder as that described in sporadic cases by Déjerine and Thomas,[13] and called by them olivo ponto cerebellar atrophy because of the prominent changes in the ventral aspects of the pons and the olivary prominences In the second familial type, described by Gordon Holmes,[14] the de eration is cerebello-fugal, it affects mainly the pa cerebellum, and there are distinct changes in the ve and in the parts of the inferior olives related anatom to the degenerated areas of the cerebellar cortex T type also has its counterpart in sporadic cases of ce bellar degeneration, and it does not differ essenti from the late cortical cerebellar atrophy described b Marie et al[15] Despite the pathological differe between the two major types of cerebellar degenerat clinically they are usually indistinguishable In b there is slow and usually progressive unsteadiness walking, followed by dysarthria and some incoordi tion of hand movements and rarely nystagmus olivo ponto cerebellar atrophy extrapyramidal ri may develop in the later stages owing to changes in *corpus striatum and substantia nigra*

The classification of these familial and sporadic de erations of the cerebellum and its connections is not of academic interest As Greenfield says "it is not all clear what is transmitted in the hereditary atax and he suggests that it may be a deficiency in cer enzyme systems in the central nervous system In ot familial neurological diseases biochemical studies h begun to yield important results The finding of ex copper deposition in hepatolenticular degeneration led to treatment by the administration of dimerca with improvement in some patients, more recently reduction of phenylalanine in the diet of children mental deficiency associated with phenylketonuria given encouraging results[16], and last week Mr Trew Dr Fischer described new evidence of disturbed d metabolic rhythm in schizophrenia[17] There is some e dence that cerebellar degeneration may be linked metabolic changes in the occasional association of sub cases with visceral carcinoma In the earlier reported c this was thought to be a chance association, but in 1 Brouwer and Biemond[18] suggested a causal relations and further reports[19 20] have supported this view most common malignant growth has been a carcino of the ovary, but in some cases there has been a bronc carcinoma and rarely a neoplasm elsewhere In cases there is diffuse loss of Purkinje cells without chan in the olives or pontine nuclei, and in some there been perivascular and meningeal lymphocytic infil tion, which Greenfield regards as secondary to the de eration rather than in any way associated with its c The clinical course is usually more rapidly progre than in the familial and sporadic degenerations, and cerebrospinal fluid may contain an excess of lymphoc with an increased protein content and a first zone La curve

SIR HENRY WADE, consulting surgeon to the Edinbu Royal Infirmary, died in Edinburgh on Monday at t age of 77

SIR GODFREY HUGGINS, F R C S, prime minister of t Federation of Rhodesia and Nyasaland, has been crea a viscount

THE INDEX and title-page to Vol II, 1954, which completed with THE LANCET of Dec 25, is publish with our present issue A copy will be sent gratis subscribers on receipt of a postcard addressed to t Manager of THE LANCET, 7, Adam Street, Adelphi, W C Subscribers who have not already indicated their de to receive indexes regularly as published should do so no

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# Social and Biological Factors in Infant Mortality *

## I THE EFFECT OF MOTHER'S AGE AND ARITY ON SOCIAL-CLASS DIFFERENCES IN INFANT MORTALITY

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HE principal object of the present inquiry is to mine social and biological factors in stillbirth and nt mortality to try to disentangle their various ts, and to observe how the factors combine In the t paper of the series[1] the familiar variation in the birth and infant mortality rates with the social class he father was briefly discussed the second paper[2] h showed that these rates also varied considerably two 'biological' factors—the age and parity of mother It is well known however, that professional ple tend to marry later and have smaller families n, say manual workers The object of the present er, therefore, is to consider the extent of such "biocal" differences between the social classes and the ct of these differences on the stillbirth and infant tality rates of the social classes The variation in the tality rates according to the occupation of the father o the part of the country in which the parents lived at time of the birth is also considered from this point iew

E I—VARIATION IN STILLBIRTH AND INFANT MORTALITY ES ACCORDING TO THE SOCIAL CLASS OF THE FATHER (Single legitimate births in England and Wales, 1949)

| ial ss | Description of occupations | Stillbirths | Neonatal † deaths | Post neonatal † deaths |
|---|---|---|---|---|
| I | Professional | 15 7 | 12 8 | 4 0 |
| II | Intermediate | 20·0 | 14 0 | 6·0 |
| III | Skilled | 21 1 | 16·0 | 10·8 |
| IV | Partly skilled | 22 6 | 18 4 | 14 4 |
| V | Unskilled | 25 7 | 19 [illegible] | 17 4 |

* Per 1000 live and still births. † Per 1000 live births
ths for which social class (or occupation) was not stated are ded from the tables in this paper unless otherwise indicated

### Analysis

s before, all observations are confined to the 691 040 le legitimate, live and still births which occurred in land and Wales in 1949 and which constituted 93% all the births in that year Multiple and illegitimate the present special problems which will be taken up er It is worth noting here that the social class of the ther or the child (or the family) is the same as the al class of the husband—which, in turn, is based on s occupation

Table I sets out the stillbirth rates and the neonatal rst four weeks) and post neonatal (remainder of first ar) mortality rates for each of the five social classes. he steady increase from social class I to social class V is n once apparent The range of variation shown is considerable, particularly for post neonatal deaths which ry from 4 0 to 17 4 per 1000 live births As was seen the second paper however the variation in the rates between mothers of different ages and parities † is also considerable post neonatal deaths there varied from 6 3 per 1000 live births (mothers of 25–29 having their first child) to 56 9 per 1000 (mothers of 20–24 having their fifth child) while stillbirth rates varied even more. The question then is: do the differences in age and parity between mothers in the various social classes account, in themselves, for an important part of the class variation in the mortality rates?

### *The Extent of the Class Differences in Age and Parity*

To illustrate the nature and extent of such differences it is simpler first of all, to consider two social classes only—those at either end of the social scale Fig 1 gives an indication of these differences showing for example that 22% of all the mothers in social class V were under 25 and having their first birth compared with 11% of all the mothers in social class I If each cell in fig 1 is assigned to one of three groups A, B and C as shown in the diagram it will be seen that A refers to those categories of age and parity where the mothers in social class V have a greater proportion of their births than the mothers in social class I; while C refers to those categories where the mothers in social class V have a smaller proportion of their births than the mothers in social class I B is an intermediate category A corresponds broadly to younger mothers and mothers with larger families C corresponds to older mothers with smaller families It can be shown that 60% of all the mothers in social class I are to be found in C compared with only 26% of all the mothers in social class V Those mothers married to professional men do therefore tend to have fewer children and to have them at a later age than the mothers married to unskilled workers The extent of these differences is considerable and it will be seen from table II that there is a steady trend throughout the social-class scale

| | | |
|---|---|---|
| A | C | C |
| A | B | C |
| A | A | A |

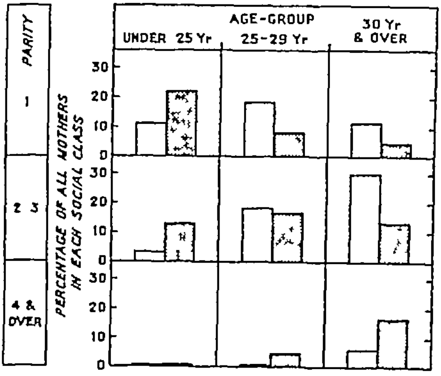

Fig 1—Distribution of mothers in nine categories of age and parity; social classes I and V compared.

Mothers having a single legitimate birth in England and Wales, 1949

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* A series of articles reporting an inquiry made jointly by the Social Medicine Research Unit (Medical Research Council) and the General Register Office The articles[1,2] were prepared by the Unit in collaboration with the General Register Office and have been approved for publication by the joint working party responsible for the inquiry

† The parity of the mother is defined here as the number of children she has borne—surviving dead or stillborn—including the present one

TABLE II—THE EXTENT OF THE SOCIAL CLASS DIFFERENCES IN AGE AND PARITY

(Single, legitimate births in England and Wales, 1949)

| Age-parity group* | Description of mothers | Social class | | | | |
|---|---|---|---|---|---|---|
| | | I | II | III | IV | V |
| A | Younger, higher parity | 22 % | 30 % | 44 % | 54 % | 57 % |
| B | Intermediate | 18 % | 18 % | 19 % | 17 % | 17 % |
| C | Older, lower parity | 60 % | 52 % | 37 % | 29 % | 26 % |
| All mothers | | 100 % | 100 % | 100 % | 100 % | 100 % |

* For description of groups see text

It is therefore necessary to "*standardise*" (or "adjust") the social class stillbirth and infant mortality rates for both mothers' age and parity (just as it is necessary to standardise the death-rates of two towns for age and sex, for example, where any comparison would otherwise be invalidated because the populations of the two towns differ in respect of these attributes) This has been done by the "direct" method, taking as the "standard population" all single, legitimate, live and still births in England and Wales in 1949 That is, in each social class, stillbirth and neonatal and post neonatal mortality-rates were calculated for each of 56 age-parity categories ‡, then, using the proportions of the standard population in these 56 categories as "weights," standardised rates were calculated as the weighted means of the 56 rates in each social class

*The Effects of the Differences*

The results of this procedure are presented in table III and fig 2, and a comparison made with the crude or unstandardised rates It is at once apparent that social-

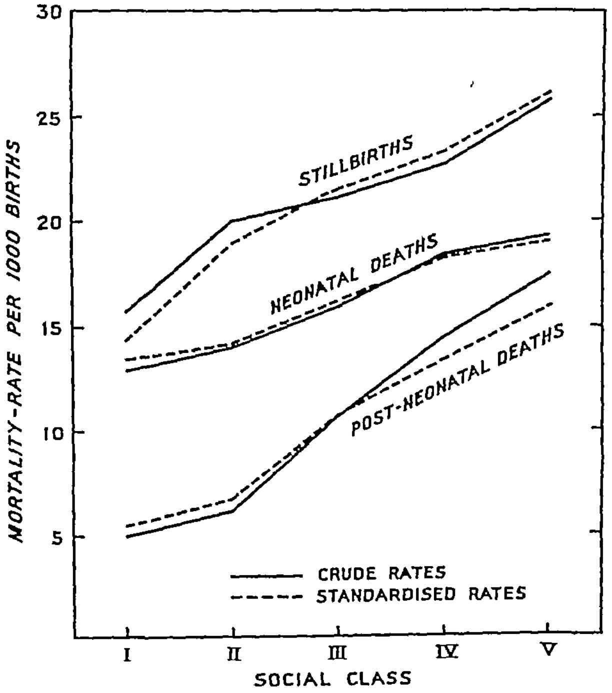

**Fig 2—Variation in stillbirth and infant mortality rates according to the social class of the father before and after standardisation for mother s age and parity**

Single, legitimate births in England and Wales, 1949

Stillbirth rates, per 1000 live and still births, other rates, per 1000 live births

class differences in age and parity have had little on the social class gradients of the mortality Standardisation has accentuated slightly the gradient stillbirths, diminished slightly the gradient for neonatal deaths, and scarcely affected that for neo deaths

Stillbirth rates have previously been corrected for and parity by other workers using similar methods[1] Their conclusions are confirmed by the present fin which, in addition, extend them to neonatal and neonatal mortality-rates Thus, although fig 2 ind that social-class differences in age and parity have a larger effect on post neonatal mortality rates tha stillbirth rates, McKinlay's conclusions are still eq applicable to all three rates "The explanation of social class differences [in foetal wastage] is to be for elsewhere than in the class differences of partu with respect to age and [previous] parity"

TABLE III—VARIATION IN STILLBIRTH AND INFANT MORT RATES ACCORDING TO THE SOCIAL CLASS OF THE FAT BEFORE AND AFTER STANDARDISATION FOR MOTHER'S AND PARITY

(Single, legitimate births in England and Wales, 194

| Social class | Description of occupations | Stillbirths* | | Neonatal† deaths | | Post-neonat deat |
|---|---|---|---|---|---|---|
| | | Crude | Standardised | Crude | Standardised | Crude |
| I | Professional | 15 7 | 14 3 | 12 8 | 13 3 | 4 9 |
| II | Intermediate | 20 0 | 18 9 | 14 0 | 14 1 | 6 0 |
| III | Skilled | 21 1 | 21 5 | 16 0 | 16 1 | 10·8 |
| IV | Partly skilled | 22 6 | 23 2 | 18 4 | 18 2 | 14 4 |
| V | Unskilled | 25 7 | 26 0 | 19 2 | 19·0 | 17 4 |
| All classes ‡ | | 21 5 | | 16 4 | | 11 1 |

* Per 1000 live and still births

† Per 1000 live births

‡ These rates are based on all births, including those where class was not stated

It is interesting to consider why standardisation had such little effect—in view of the fact that the mortality-rates vary considerably with mother's age parity, and the various social classes also differ siderably with respect to both of these factors, so quite substantial changes with standardisation well have been expected An important reason for is the fact that only a very small proportion of mo are exposed to the high mortality risks occasioned unfavourable age or parity It was pointed out in second paper[2] that babies of the younger mothers large families for their age have a high risk of death the post neonatal period But if this group is taken to be second or later births to mothers aged 16–19, or later births to mothers aged 20–24, and also fifth later births to mothers aged 25–29, it is found that births constitute only 3 7% of all live births in 19 Similarly, mothers over 35 bearing their first baby, all mothers over 40, have a high risk of stillbirth the number of births to these mothers was only 5·8 of all births in 1949 It will be seen, therefore, although there appears to be a very great range variation in the mortality-rates when mothers of differ ages and parities are considered, the overwhelming majority of mothers are not affected by the extreme rate Only if the above proportions had been increased fi fold, at least, would standardisation for age and parity have had any marked effect

Since the grouping of occupations into broad so classes is bound, in itself, to reduce the range of variat of the mortality-rates, it is interesting to examine effects of standardisation on the rates for those occu tional groups shown in table IV It will be seen that differences between the crude and standardised rates portion r, rather ter than social ses, and agam the neonatal tality are most ted. The test indi al change icerns enior rical kers"— ng clerks l bank rks, for mple— re the dardised -neonatal mortality rate of 6 7 per 1000 live births is greater than the corresponding crude rate of 5 2 per When it is realised however that the children of neworkers (coal) in class IV —that is the semi d workers—have a crude post-neonatal mortality almost five times as high as this it is clear that age parity differences between the wives of men in these pational groups play little part in accounting for large differences in the mortality rates of their dren

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‡ The 56 age parity categories were obtained by considering
(1) Mothers aged 16–19, 20–24 25–29 30–34, 35–39 40–44 45 and over, and "age not stated.
(2) Mothers of parity 1, 2, 3, 4 5, 6 and over and parity not stated '

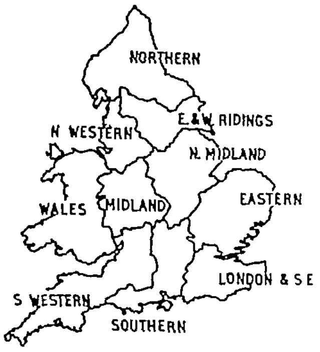

Fig 3—The ten " standard regions " of England and Wales.

ifferent parts of the country, it is well known have ifferent stillbirth and infant mortality experience table V sets out the relevant rates—before and after dardisation—for the ten standard regions' of land and Wales shown in fig 3 Most of the crude rates presented in this table are hardly affected by standardisation the greatest individual change is for the post neonatal mortality rate in the Northern region—and here the standardised rate is only 5% less than the crude rate Since the crude post-neonatal mortality rate for the Eastern region is less than half the crude rate for the Northern region it is easy to conclude that the differences in the regional rates must certainly be ascribed to causes other than any tendency there may be for mothers in the various regions to differ in respect of age and parity This means, for instance, that we cannot attribute the traditionally high stillbirth rate in Wales to differences in age or family size between mothers in Wales and mothers in England

LE IV—VARIATION IN STILLBIRTH AND INFANT MORTALITY TES ACCORDING TO THE OCCUPATION OF THE FATHER FORE AND AFTER STANDARDISATION FOR MOTHER S AGE D PARITY

(Single legitimate births in England and Wales 1949)

| Occupation | Still births | | Neo natal† deaths | | Post neonatal† deaths | |
|---|---|---|---|---|---|---|
| | Crude | Standardised | Crude | Standardised | Crude | Standardised |
| Professional workers | 15·7 | 14·3 | 12·8 | 13·3 | 4·9 | 5·4 |
| Farmers | 23·8 | 22·4 | 14·4 | 14·0 | 7·6 | 7·4 |
| Senior clerical workers | 16·9 | 16·2 | 11·0 | 11·6 | 5·2 | 6·7 |
| All others in social class II | 19·7 | 18·5 | 14·4 | 14·5 | 5·9 | 5·7 |
| Coal hewers and getters | 25·8 | 26·0 | 19·5 | 20·5 | 19·0 | 17·2 |
| Transport workers | 21·9 | 22·3 | 17·1 | 17·6 | 11·1 | 11·0 |
| Clerical workers | 20·8 | 20·6 | 13·7 | 14·0 | 8·3 | 7·8 |
| Armed Forces | 18·3 | 20·1 | 16·4 | 16·3 | 11·7 | 10·4 |
| All others in social class III | 20·0 | 21·2 | 15·7 | 15·8 | 10·2 | 10·4 |
| Agricultural workers | 19·5 | 19·2 | 16·9 | 16·5 | 9·3 | 8·7 |
| Mineworkers (coal) in social class IV | 22·5 | 23·8 | 23·4 | 22·7 | 23·9 | 21·3 |
| All others in social class IV | 23·7 | 24·5 | 17·7 | 17·8 | 13·9 | 13·1 |
| Building labourers | 23·5 | 24·4 | 18·9 | 19·0 | [illegible] | 18·1 |
| Dock labourers | 29·9 | 27·4 | [illegible] | 16·1 | 18·1 | 14·5 |
| All others in social class V | 26·1 | 26·4 | 19·5 | 19·1 | 16·6 | [illegible] |

Per 1000 live and still births. † Per 1000 live births

Transport workers clerical workers, Armed Forces and agricul al workers are occupations defined by the General Register as "functional subdivisions" of the social classes The occupations listed above where not otherwise obvious are ed by the following code numbers farmers (010 011 0[illegible]0) ior clerical workers (611 61[illegible] 893), coal hewers and getters 1, 012); building labourers (58[illegible] 5[illegible]1 580 591 599) dock ers (641).

## Comment

The present analysis shows that it would be wrong to attribute any important part of the social class occupational and regional differences in the stillbirth and infant-mortality rates of England and Wales to differences in the ages and parities of the mothers concerned This raises the question of the independence of action of the factor of social class (or occupation, or region) and the factors of age and parity For instance is a social class effect present whenever a group of mothers of a particular age and a particular parity is considered or conversely is an age parity effect present whenever mothers in a particular social class are considered ? That independence of action (as thus defined) does indeed exist will be demonstrated in the next paper of this series.

TABLE V—VARIATION IN STILLBIRTH AND INFANT MORTALITY RATES ACCORDING TO THE PART OF THE COUNTRY IN WHICH THE PARENTS LIVED AT THE TIME OF THE BIRTH : BEFORE AND AFTER STANDARDISATION FOR MOTHER S AGE AND PARITY

(Single legitimate births in England and Wales, 1949)

| Standard regions | Stillbirths* | | Neonatal† deaths | | Post neonatal† deaths | |
|---|---|---|---|---|---|---|
| | Crude | Standardised | Crude | Standardised | Crude | Standardised |
| Northern | 23·4 | 23·0 | 18·5 | 18·4 | 17·9 | 17·0 |
| East and West Ridings | 22·0 | 21·9 | 17·6 | 17·6 | 12·9 | 12·7 |
| North Western | 24·3 | 24·3 | 17·8 | 17·8 | 14·7 | 14·6 |
| North Midland | 21·0 | 21·1 | 15·9 | 16·0 | 11·6 | 11·3 |
| Midland | 22·0 | 22·0 | 16·7 | 16·7 | 12·3 | 12·0 |
| Eastern | 19·8 | 20·0 | 13·7 | 13·8 | 7·0 | 7·0 |
| London and South East | 18·7 | 18·6 | 14·3 | 14·1 | 7·6 | 7·9 |
| Southern | 18·2 | 18·5 | 14·8 | 14·8 | 7·1 | 7·1 |
| South Western | 21·1 | 21·3 | 17·3 | 17·4 | 7·9 | 7·9 |
| Wales | 27·0 | 26·8 | 19·3 | 19·2 | 14·0 | 13·5 |

Per 1000 live and still births † Per 1000 live births

Finally it is worth pointing out that the above results should not be taken to mean that age and parity need never be considered in any discussion of social' effects Differences in age and parity may well be important for instance in any comparison of legitimate and illegitimate mortality rates (since illegitimate births are so frequently first births to young mothers) and in comparisons of countries which have substantially different age parity patterns

## Summary

It is shown that there were considerable differences between the social classes in the ages and parities of those mothers who had a single legitimate birth in England and Wales in 1949 It is then demonstrated however that the explanation of the variation between the classes in the stillbirth rate the neonatal (first four weeks of life) mortality rate and the post neonatal (remainder of first year of life) mortality rate must be looked for elsewhere than in these age and parity differences Similar conclusions are reached in the case of differences in the mortality rates when analysed according to the occupation of the father or according to the region of England

and Wales in which the parents lived at the time of the birth

We are grateful to the staff of the General Register Office for professional, technical and computing help, to colleagues for criticism and advice, particularly to Mr C F Stevens, and to the staff of the Social Medicine Research Unit for clerical and computing work

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CORRIGENDUM—In the last compartment of fig 1 of paper II in this series (*Lancet*, Feb 19, p 395) the figure for Parity 1 should be where "2, 3" are at present, and vice versa

# Special Articles

## CONSULTANT AND OTHER SPECIALIST STAFF IN HOSPITALS

THE accompanying tables have been issued by the Ministry of Health and Department of Health for Scotland as being of interest to the medical profession generally, and especially perhaps to those intending to train as specialists All the figures relate to National Health Service hospitals in Great Britain

TABLE III—NUMBER OF SENIOR REGISTRARS IN EACH SPECIALTY IN 1954 (GREAT BRITAIN)

| Specialty | Training plan | | | | | Others |
|---|---|---|---|---|---|---|
| | 1st yr | 2nd yr | 3rd yr | 4th yr | Total | |
| General medicine | 44 | 33 | 25 | 22 | 124 | 7 |
| Diseases of the chest | 24 | 18 | 4 | 9 | 55 | 16 |
| Mental health | 51 | 29 | 12 | 10 | 102 | 27 |
| Neurology | 3 | 3 | 5 | 4 | 15 | 4 |
| Pædiatrics | 11 | 5 | 7 | 1 | 24 | 17 |
| Radiology | 28 | 21 | 8 | 4 | 61 | 1 |
| Radiotherapy | 5 | 7 | 2 | 3 | 17 | [illegible] |
| Physical medicine | 4 | 3 | 2 | 1 | 10 | [illegible] |
| Pathology | 21 | 21 | 14 | 7 | 63 | 2 |
| Infectious diseases | 2 | 2 | | | 4 | 3 |
| Dermatology | 2 | 6 | 6 | 8 | 22 | 10 |
| Venereology | 3 | 1 | | 1 | 5 | 4 |
| Ophthalmology | 12 | 14 | 9 | 11 | 46 | 11 |
| General surgery | 50 | 40 | 24 | 20 | 134 | 69 |
| Anæsthetics | 31 | 15 | 12 | 1 | 59 | 8 |
| Neurosurgery | 2 | 5 | | 5 | 12 | 5 |
| Plastic surgery | 2 | 2 | 6 | 4 | 14 | 3 |
| Thoracic surgery | 8 | 3 | 3 | 4 | 18 | 1* |
| Orthopædic surgery | 13 | 14 | 13 | 10 | 50 | 12 |
| Ear, nose, and throat surgery | 13 | 12 | 8 | 2 | 35 | 13 |
| Obstetrics and gynæcology | 26 | 15 | 17 | 13 | 71 | 35 |
| Others | 1 | | | 1 | 2 | 1 |
| Totals | 356 | 209 | 177 | 141 | 943 | 363* |

* Includes 61 honorary and 41 part time senior registra

Table I shows the age distribution in 1954 of co tants and senior hospital medical officers practis the various specialties (Some, especially those

TABLE I—AGE-DISTRIBUTION IN 1954 OF CONSULTANTS AND S.H.M.O.S IN EACH SPECIALTY (GREAT BRITAI

| Year of birth | Specialty | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | General medicine | Diseases of the chest | Mental health | Neurology | Pædiatrics | Radiology | Radiotherapy | Physical medicine | Pathology | Infectious diseases | Dermatology | Venereology | Ophthalmology | General surgery | Anæsthetics | Neurosurgery | Plastic surgery | Thoracic surgery | Orthopædic surgery | Ear, nose and throat surgery | Obstetrics and gynæcology | Miscellaneous | Totals |
| 1883 | | | | | | | | | 1 | | | | | 1 | | | | | | | | | 2 |
| 1884 | 1 | | | | | | | | 1 | | | 1 | 1 | 1 | 1 | | | | | | | | 6 |
| 1885 | 1 | | | 2 | | | | | | | | | | 5 | | | | | 1 | 1 | | | 10 |
| 1886 | 2 | | | | | 3 | | | 2 | | | | 1 | 3 | 1 | | | | 1 | 1 | | | 14 |
| 1887 | 1 | | 1 | | | | | 1 | 2 | | | 1 | 5 | 3 | | | | | 1 | 2 | | | 17 |
| 1888 | 7 | 6 | 1 | 1 | 1 | 5 | | | 7 | 2 | | 2 | 2 | 1 | 2 | | | | 1 | 2 | 3 | | 43 |
| 1889 | 11 | 5 | 2 | | | 9 | | | 8 | 2 | 1 | 2 | 6 | 17 | 4 | 1 | | 1 | 3 | 5 | 8 | | 85 |
| 1890 | 13 | 2 | 15 | 3 | 1 | 6 | 1 | 1 | 6 | 1 | 5 | 1 | 3 | 16 | 8 | 1 | 1 | 1 | 4 | 5 | 5 | | 99 |
| 1891 | 18 | 2 | 3 | | 2 | 8 | 1 | 1 | 9 | 3 | 3 | 3 | 7 | 23 | 2 | | | | 3 | 4 | 11 | | 103 |
| 1892 | 11 | 9 | 9 | | 8 | 10 | | 3 | 6 | 3 | 3 | 3 | 11 | 20 | 8 | | | | 5 | 8 | 7 | | 124 |
| 1893 | 24 | 7 | 10 | 1 | 3 | 11 | 2 | | 7 | 4 | 3 | 3 | 17 | 24 | 12 | | | 2 | 1 | 7 | 6 | | 144 |
| 1894 | 16 | 9 | 13 | | 2 | 8 | | | 12 | 5 | 7 | 6 | 15 | 23 | 13 | | | | 4 | 8 | 10 | 1 | 151 |
| 1895 | 20 | 12 | 13 | 1 | 3 | 11 | | 1 | 18 | 5 | 1 | 2 | 10 | 22 | 15 | | | 1 | 2 | 9 | 11 | | 157 |
| 1896 | 23 | 8 | 19 | 1 | 5 | 11 | 3 | 1 | 16 | 5 | 8 | 7 | 15 | 28 | 20 | | 1 | 1 | 4 | 13 | 10 | | 205 |
| 1897 | 32 | 11 | 27 | 1 | 4 | 14 | 3 | 2 | 14 | 3 | 6 | 7 | 11 | 37 | 29 | 2 | | 1 | 7 | 12 | 13 | | 236 |
| 1898 | 31 | 10 | 30 | | 6 | 17 | 3 | 1 | 14 | 6 | 9 | 7 | 24 | 27 | 25 | | | | 4 | 11 | 21 | | 246 |
| 1899 | 27 | 16 | 35 | 4 | 2 | 17 | 7 | 8 | 24 | 6 | 6 | 4 | 30 | 50 | 32 | 1 | | | 7 | 12 | 17 | | 305 |
| 1900 | 48 | 24 | 42 | 2 | 10 | 14 | 4 | 3 | 17 | 11 | 11 | 8 | 28 | 51 | 45 | 3 | 1 | 1 | 16 | 22 | 16 | | 377 |
| 1901 | 41 | 20 | 34 | | 5 | 21 | 4 | 3 | 18 | 13 | 8 | 6 | 29 | 42 | 37 | | 2 | 1 | 10 | 26 | 19 | | 339 |
| 1902 | 29 | 32 | 34 | 5 | 12 | 12 | 3 | 3 | 10 | 5 | 1 | 10 | 21 | 54 | 42 | 3 | 3 | 4 | 14 | 19 | 24 | | 340 |
| 1903 | 38 | 27 | 30 | 5 | 6 | 11 | 3 | 2 | 22 | 5 | 7 | 5 | 18 | 49 | 38 | | 2 | 4 | 12 | 9 | 23 | | 316 |
| 1904 | 40 | 21 | 32 | 3 | 5 | 10 | 4 | 2 | 17 | 4 | 5 | 5 | 14 | 57 | 29 | 1 | 1 | | 11 | 14 | 21 | | 296 |
| 1905 | 35 | 26 | 42 | 1 | 6 | 13 | 3 | | 25 | 1 | 5 | 11 | 23 | 38 | 32 | 1 | 1 | 3 | 8 | 10 | 18 | | 302 |
| 1906 | 37 | 20 | 42 | 1 | 7 | 11 | 3 | 6 | 22 | 5 | 6 | 5 | 12 | 47 | 30 | 3 | 1 | 2 | 12 | 13 | 16 | | 309 |
| 1907 | 63 | 27 | 38 | 6 | 11 | 10 | 2 | 3 | 20 | 4 | 9 | 6 | 10 | 38 | 27 | 1 | 4 | 3 | 25 | 12 | 26 | | 360 |
| 1908 | 43 | 20 | 40 | 4 | 11 | 10 | 6 | 3 | 22 | 5 | 8 | 6 | 19 | 46 | 41 | 2 | 3 | 3 | 19 | 12 | 18 | | 341 |
| 1909 | 49 | 22 | 31 | 6 | 14 | 13 | 3 | 3 | 27 | 3 | 4 | 4 | 22 | 39 | 33 | 4 | 2 | 3 | 22 | 15 | 28 | | 347 |
| 1910 | 52 | 26 | 39 | 2 | 15 | 20 | 5 | 3 | 35 | 2 | 10 | 9 | 24 | 68 | 32 | 3 | 1 | 4 | 22 | 13 | 27 | | 412 |
| 1911 | 49 | 42 | 43 | 2 | 7 | 14 | 9 | 4 | 30 | 5 | 8 | 8 | 18 | 47 | 38 | 1 | 5 | 6 | 23 | 16 | 31 | | 406 |
| 1912 | 45 | 23 | 46 | 2 | 11 | 28 | 4 | | 43 | 5 | 8 | 4 | 13 | 60 | 41 | 2 | 2 | 6 | 19 | 10 | 34 | | 398 |
| 1913 | 52 | 42 | 39 | 3 | 9 | 25 | 11 | 5 | 35 | 4 | 8 | 5 | 18 | 57 | 40 | 5 | 2 | 4 | 24 | 14 | 32 | | 440 |
| 1914 | 55 | 41 | 46 | 2 | 10 | 29 | 12 | 4 | 49 | 5 | 8 | 7 | 23 | 50 | 46 | 2 | 1 | 7 | 18 | 10 | 20 | | 451 |
| 1915 | 60 | 44 | 48 | 5 | 14 | 26 | 4 | 7 | 49 | 2 | 8 | 7 | 24 | 34 | 60 | 4 | 6 | 6 | 20 | 14 | 30 | | 481 |
| 1916 | 52 | 53 | 42 | 3 | 17 | 31 | 6 | 5 | 41 | 5 | 5 | 3 | 22 | 47 | 40 | 4 | 2 | 6 | 19 | 13 | 21 | | 448 |
| 1917 | 34 | 28 | 36 | 4 | 13 | 17 | 11 | 4 | 41 | 1 | 1 | 3 | 22 | 20 | 55 | 2 | 3 | 8 | 17 | 12 | 17 | | 355 |
| 1918 | 20 | 33 | 24 | | 16 | 18 | 10 | 10 | 35 | 1 | 12 | 2 | 14 | 20 | 38 | | 2 | 6 | 9 | 10 | 11 | | 291 |
| 1919 | 28 | 22 | 28 | 2 | 6 | 20 | 9 | 3 | 32 | 1 | 7 | 2 | 13 | 14 | 24 | 2 | | 2 | 8 | 9 | 9 | 1 | [illegible] |
| 1920 | 19 | 24 | 31 | | 4 | 14 | 4 | 1 | 33 | | 4 | 4 | 8 | 8 | 40 | 1 | | 2 | 4 | 3 | 4 | | 205 |
| 1921 | 5 | 17 | 10 | | 1 | 13 | 4 | 1 | 18 | 1 | 1 | 2 | 9 | 2 | 28 | | | 3 | 2 | 7 | 2 | | 126 |
| 1922 | 3 | 13 | 15 | 1 | 1 | 7 | 5 | | 7 | 2 | | | 8 | | 27 | | | 1 | | 3 | | | 93 |
| 1923 | 1 | 8 | 7 | | | 4 | 1 | 1 | 4 | | | 1 | 8 | | 11 | | | | | 1 | | | 47 |
| 1924 | 3 | 1 | | | | | 1 | | 2 | | | | 5 | | 7 | | | | | | | | 19 |
| 1925 | 1 | 2 | 2 | | | | | | | | | | 3 | 1 | 1 | | | | | | | | 10 |
| 1926 | | 1 | 1 | | | | | | | | | | 1 | | 1 | | | | | | | | 4 |
| 1927 | | | | | | | | | | | | | 1 | | | | | | | | | | 1 |
| Totals | 1139 | 756 | 1000 | 73 | 248 | 521 | 151 | 95 | 810 | 135 | 196 | 172 | 594 | 1189 | 1082 | 40 | 46 | 92 | 391 | 387 | 580 | 2 | 9708 |

Consultants and S.H.M.O.s practising in more than one specialty have been included under each

TABLE II—NUMBERS OF CONSULTANTS IN EACH SPECIALTY AT VARIOUS DATES SINCE DEC. 31 1949 (GREAT BRITAIN)

| ate | Specialty | | | | | | | | | | | | | | | | | | | | | Totals | Date |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | General medicine | Diseases of the chest | Mental health | Neurology | Paediatrics | Radiology | Radiotherapy | Physical medicine | Pathology | Infectious diseases | Dermatology | Venereology | Ophthalmology | General surgery | Anaesthetics | Neurosurgery | Plastic surgery | Thoracic surgery | Orthopaedic surgery | Ear nose and throat surgery | Obstetrics and gynaecology | | |
| 1 1949 | 755 | 216 | 449 | 58 | 166 | 327 | 85 | 19 | 495 | 50 | 12 | 69 | 331 | 927 | 496 | 37 | 30 | 40 | 252 | 312 | 424 | 5719 | Dec. 31 1949 |
| 31 1950 | 831 | 250 | 504 | 53 | 202 | 378 | 93 | 57 | 526 | 52 | 136 | 101 | 311 | 943 | 602 | 39 | 32 | 57 | 269 | 328 | 430 | 6233 | Dec 31 1950 |
| 31, 1951 | 857 | 266 | 532 | 59 | 208 | 400 | 101 | 61 | 541 | 48 | 13 | 99 | 342 | 948 | 656 | 12 | 33 | 66 | 303 | 341 | 449 | 6476 | Dec. 31 1951 |
| 31, 1952 | 904 | 310 | 566 | 61 | 214 | 414 | 108 | 70 | 581 | 61 | 142 | 97 | 351 | 986 | 714 | 44 | 36 | 81 | 320 | 339 | 473 | 6862 | Dec 31 1952 |
| 31 1953 | 905 | 340 | 585 | 67 | 222 | 436 | 112 | 75 | 631 | 60 | 145 | 94 | 349 | 982 | 748 | 46 | 43 | 89 | 328 | 346 | 473 | 7079 | Dec 31 1953 |
| 30 1954 | 910 | 341 | 600 | 66 | 225 | 439 | 113 | 74 | 634 | 60 | 147 | 95 | 338 | 986 | 767 | 48 | 45 | 90 | 330 | 348 | 477 | 7136 | June 30 1954 |

Consultants practising in more than one specialty have been included under each

age-groups have contracts for only a small number essions and it therefore does not follow that retirement will provide a vacancy for a new it.)

ble II shows the increase in the number of con ants in each of the specialties between the end of and June 30 1954 The corresponding figures for r hospital medical officers are not available

ble III shows the number of senior registrars in each alty in 1954 at the various stages of their training column headed ' Others includes those holding nsitional ' posts.

## TEACHING MENTAL HEALTH

### iscussion by the Royal Medico Psychological Association

L agree that the time has come to dispel the old superstitious dread of mental illness to overcome and prejudice about mental hospitals, and to teach w straightforward principles of mental hygiene when the Royal Medico Psychological Association on Feb 17 to discuss the education of the general c in mental health it was instructive to see how ently well informed people could view this field of . While some speakers examined the foreground unaided eye others seemed to be looking through copes pointed in all directions Miss PAT HORNSBY H, M.P., parliamentary secretary to the Ministry ealth, belonged to the first group We tend to ignore and, the amazing ignorance of the public about the mind and the work of the mental hospitals The ernment must have public support in order to spend ey on a mental health programme it cannot spend ey successfully unless staff can be attracted to the ice and the service cannot reduce acute mental s unless patients can be persuaded to come early treatment. The public must be helped to understand nursing the sick mind is as important as nursing ick body and to recognise the dramatic change which come about in prospects of recovery for the mentally Few know that nearly 70% of those admitted to tal hospitals are nowadays voluntary patients or the annual turnover of patients is now about 40% y do not distinguish between the mentally ill and the tally defective or between the psychotic and the otic and their ideas of mental hospitals are still to be coloured by the terms padded cells' and ing put away ' Psychiatrists she suggested whether ugh fear or foible, are reluctant to write or speak to general public in simple terms about these things moment they use words which everyone can under d, they start looking over their own shoulders and wondering what their colleagues will think of them Yet it is much better that those who know should tell the facts about mental illness and explain that mental hospitals are not places where people are shut up but where they are treated. Nothing but good, she urged can come of holding open days ' at mental hospitals: bring in the unconverted bring in talkative public opinion Once these critics have seen for themselves that things are much better then they expected they will go and talk about it to others. The press and the British Broadcasting Corporation can play a vital part she thinks if they are given skilled guidance by the medical profession Local programmes arranged by the local authorities and bringing in voluntary bodies and the general public can foster the interest in mental health which is growing all over the country Study groups should be set up and lectures given by psychiatrists We shall not be able to attract enough nurses ' until we have the press, the public, and the parents with us ' and the way to win them over is to let them in to see the mental hospitals We must also she said convince some of the old fashioned members of the nursing profession that mental nursing is just as important as general nursing the mental nurse must have a higher status in her own profession She reminded the meeting that despite shortage of buildings shortage of staff, and overcrowding we are still ahead of most other nations in our care of the mentally sick we must keep that lead

Dr R R BOMFORD who had been asked to speak as a non psychiatric doctor ' made it clear that there was an opportunity for mental health education not only in his group but among psychiatrists too Have you the knowledge ' he asked his psychiatric colleagues ' to prevent mental ill health ? Drains clean water and better houses we know have done much to prevent physical ill health What are the equivalents for mental hygiene ? Again what is psychiatry and what is a psychiatrist ? There are so many different methods in psychiatry that the non psychiatric doctor is apt to be puzzled and many of the exponents of these methods seem to confuse theory with verified fact. What sort of evidence is to be accepted ? Uncritical acceptance of psychiatric theories is dangerous and uncritical abuse of them is irrational. The concept that ' conflict causes disease ' is an oversimplification No illness has a single cause most physicians are well aware of the effects of emotion in patients and know that certain illnesses are more liable to develop in people of a given tempera ment or a given physique and that any illness is affected by the patient s emotional and social circumstances The evidence that an illness can be caused by a conflict is not Dr Bomford thinks satisfactory As long as the non psychiatric doctor continues to abuse and the psychiatrist continues to lecture we shall not he thinks, get very far They must examine and elucidate their differences of outlook The younger generation of doctors are showing an interest in the subject, and time will bring about an understanding

Dr W S Maclay fortified Dr Bomford's misgivings In teaching mental health, he said, we should be on firmer ground if we knew what we wanted to teach "Tell us what to do, and we'll do it," the public, the health administrators, and the politicians all cry to the psychiatrist, but he does not know He knows that people are influenced by their upbringing, but what is a proper upbringing? The anthropologists tell us of some cultures in which upbringing produces a peace-loving people, and others in which the upbringing produces people who are warlike and aggressive Which is "right"? Or how does one achieve a happy mixture of the two? Our programme for mental health contains various practical measures We want to provide enough mental hospital beds, early diagnosis and treatment for individuals, the means for rehabilitation of patients leaving hospital (links with the local authorities and voluntary organisations), and consultative services (available to courts, resettlement units, remand homes, and the like) We also want to prevent those mental disorders where the ætiology is clear—by means of better obstetrics, better control of venereal disease, control of infections with antibiotics, good nutrition (to prevent those mental disorders, such as pellagra, which are caused by nutritional deficiencies), and even the wider use of crash helmets and the better control of boxing matches When it comes to preventing mental disorders with psychological causes we need far more information than we have at present We need to know, for instance, more about the effects on children of cruelty, broken homes, lack of affection, and separation from parents In the education of the public, teachers, social workers, and clergy may be more important than psychiatrists the wives of psychiatrists, he had noticed, have on the whole very little respect for their husband's views on the upbringing of children Will it be useful to try to influence the public through radio, television, lectures, discussion groups, plays, and films? Can behaviour (which may be deeply rooted in the personality) be readily changed through these channels? We need more research into educational methods We also need a much fuller study of sound mental health, to determine which infants need cuddling, which schoolboys will benefit from a beating, which adults need marriage guidance, and so on "Mental health" cannot be applied to a vague mass, "the public," but only to individuals, based on respect and affection

Mr François Lafitte, who owned himself to be both non-psychiatric and non doctor, shared Dr Maclay's pessimism about using the press and other media for mass education The first thing surely, he said, is to get over some simple facts—the psychiatrists to decide which The press is a part of the public which *needs* educating, and on the whole journalists are receptive and intelligent what they need are opportunities to see for themselves what mental hospitals are doing Films and broadcasting, however, are likely to have a more lasting influence on the general public than newspapers There is a danger that by harping too much on hospital beds and curative treatment we may create in the public a new demand for psychiatry—an appetite for treatment—which we might not be able to meet He suggested that we might do better by emphasising the factors making for good mental health—*such as sensible child management* and harmonious marriage relations Is there a case, he asked, for teaching simple psychology in schools? The public are semi-ignorant about the body and still more ignorant about the mind might not both have a place in the school curriculum?

In the ensuing discussion Dr J Ffoulkes Edw
felt we might be optimistic about teaching mental he
and mentioned a postgraduate course in health educ
now being held by ,the University of London—the
of its kind—to train people for giving such teach
Those attending the course are nurses, teachers, or doc
over the age of 30 There is a great opportunity,
thinks, for teaching mental health principally in
schools the old are hard to change, but there is h
*with the young*

The value of training ordinary social workers in
principles of mental hygiene was mentioned by an
speaker they can change public opinion indirectly,
save us from the mistakes which may come of tak
it directly On this note of scientific caution the me
almost expired, but a final speaker urged, wi
much apparent effect, the essence of Miss Ho
Smith's discourse—that the removal of old m
ceptions is surely a task worth tackling

## THE HEALTH OF THE ARMY

In no section of the community may the princip
preventive medicine be so vigorously or effect
applied as in the fighting Services, and the repo
the Health of the Army for 1951 and 1952[1] co
that full advantage is being taken of this opport
Since all but the most trivial conditions are treat
medical reception stations or hospitals, a reaso
accurate index of morbidity is afforded by figure
admissions to Army medical units, and these, even
the two years covered by this report, show a remark
decrease

Not surprisingly, each command has a
peculiar to itself the admission-rate in Korea and Jap
1952 was nearly 50% higher than that in Farelf—
in turn, was some 25% higher than in B.A O R
1951, when the Korean campaign was getting under
admission rates there totalled 1121 per 1000 perso
the following year, when some of the health pro
had been successfully solved, the figure dropp
788 per 1000

The major causes of admission in the United King
were tonsillitis and pharyngitis, skin conditions, and
common cold—in that order In M E.L.F, on the
hand, skin conditions greatly exceeded any other
dition as a cause of admission In Farelf, and in
and Japan, venereal disease was the principle ca
admission In the latter command venereal d
accounted for no fewer than 387 admissions per
personnel in 1951, and 262 the following year,
action accounted for only 85 7 (1951) and 42 7 (
admissions per 1000 personnel

Of deaths reported from or certified in a me
unit in 1952, 7 1% were due to tuberculosis, 23 2
neoplasms, 11 0% to cardiac conditions, 9 0% to cere
vascular lesions, and 5 2% to poliomyelitis or p
*encephalitis* Tuberculosis deaths totalled 11, comp
with 131 in 1948 Accidents accounted for 329 dea
and enemy action for 35 deaths

During the two years no major changes were made
the physical standards of entry to the Regular
Territorial Army Nevertheless, the principle *that a*
*a man fit in all respects can make a useful soldier*
being replaced by one which recognises that men w
appreciable physical limitations can be usefully emplo
in sedentary duties or under certain strictly def
conditions As a result of this change of policy,
*more immediately*, because of the serious shortage
man-power in the spring of 1951, some men were recr
whose physical category would formerly have deba
them from the Service

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[1] Report on the Health of the Army 1951 and 1952 Not co
but copies have been distributed to learned societies

## 'LUORIDATION OF WATER-SUPPLIES

HE Board of Faculty of Dental Surgery of the Royal ege of Surgeons of England was asked by the Minister Iealth to consider fluoridation of domestic water lies in the control of dental caries The following rt, prepared by Prof H H Stones and Prof M A hton, has been approved for submission to the ister

he board are satisfied that the incidence of dental s is much less among children and adults who have t the whole of their prenatal and postnatal life reas where the drinking water naturally contains ide at a level of one part per million or more than ng those in areas where the water is practically free fluoride

1945 the fluoridation of domestic water-supplies reducing the incidence of dental caries was started rtain selected communities in the United States of rica, and in one in Canada Eight of these com ities in which fluoridation was started from 1945 to have been used as study centres The results ined each year have been compared with the base data; and in some centres, as an additional control al examinations have been undertaken in adjoining comparable communities.

he evidence to date shows a reduction in dental s incidence of 40–50% in children of the youngest groups which is comparable to what is observed in s where the water has naturally a fluoride content ne part per million or more In the older age groups teeth have not been subjected to fluoridation during their formative period, and the reduction is not as yet so marked There is nothing to suggest that a water naturally containing fluoride has properties different from those to which fluoride has been added

In a temperate climate having a population of adequate nutritional standard fluoride at a concentration of 1–1 5 parts per million as fluorine in the water produces an occasional white fleck on the enamel, but this cannot be detected without expert dental examination and is found in only about 10% of children The appearance of the teeth is excellent

There is no scientific evidence of toxicity or of harmful effects in districts with the water supply fluoridated at this level

The board considers that there is very strong evidence in support of fluoridation and welcomes the proposal that this procedure should be adopted in the first place in some selected districts that can be used as study centres

## SCOTTISH STANDING ADVISORY COMMITTEES

THE Secretary of State for Scotland has appointed new members to the standing advisory committees to hold office until Dec 31 1957 and has reappointed other members whose terms of office have expired Medical members have been appointed or reappointed as follows

*Nursing and Midwifery Advisory Committee*—Dr G J Summers (Barnton)

*Advisory Committee on Local Authority Services*—Dr Richard Scott (Edinburgh)

*Advisory Committee on Health Services in the Highlands and Islands*—Dr Angus Lamont (Foyers) Dr Thomas Scott (Inverness)

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# Parliament

### Committee on Medical Man-power

Feb 21, in answer to a question Mr IAIN MACLEOD, Minister of Health announced that, with the Secre- of State for Scotland, he was setting up a committee estimate, on a long term basis and with due regard ll relevant considerations, the number of medical itioners likely to be engaged in all branches of the ession in the future, and the consequential intake of ical students required The committee would be r the chairmanship of Mr Henry Willink Q C, the other members would be

T BALDWIN M B Sir HAROLD BOLDERO F.R.C.P JOHN CHARLES F.R.C.P Sir HENRY COHEN F.R.C.P ANDREW DAVIDSON F R.C.P.E A. B DAVIES M.B P DODDS, Sir GEOFFREY JEFFERSON F.R.C.S F.R.S., K. STARKE, F.I.A A B TAYLOR D.LITT The secretary ld be P V Muston of the Ministry of Health

### N.H.S Supplementary Estimates

On Feb 16 supplementary estimates for the health vice in England and Wales and Scotland[1] were ented in the House of Commons In introducing the plementary estimate of £4 818 000 for England and les Miss PATRICIA HORNSBY-SMITH parliamentary etary to the Ministry of Health said that the largest m was for hospital maintenance She paid tribute to good use the hospital authorities were making of money made available to them and pointed out that t year there had been an increase of 8000 in the daily erage of occupied hospital beds, of 125 000 in new patients, and of 277 000 in casualty attendances.

#### MEDICINE GALORE

The next major item was for the pharmaceutical vice This was mainly due to an increase in the erage cost of a prescription which was now 4s 2½d mpared with 4s. 1d. in 1953–54 An increase of 4½ lion prescriptions was expected The supplementary timate for the dental services was due to an all time record for conservative treatment—6 million patients had been treated compared with 5 400 000 in 1953–54 and those treated under 21 rose from 2,000,000 in 1953–54 to 3 million last year

Mr H A MARQUAND asked for further details of the cause of the rise in the average cost of prescriptions Mr IAIN MACLEOD Minister of Health, interposed that during the year two expensive drugs, aureomycin and terramycin had been made freely prescribable Mr MARQUAND agreed that expensive drugs were often better value for money than the less expensive ones But he asked for more information about the Minister's attack on the prices of 91 proprietary articles which accounted for 18% of the total drug bill Would it not, he suggested be a real economy to attract pharmacists back from outside trade and build up a good hospital pharmaceutical service? Salary adjustment alone would do this.

Sir HUGH LINSTEAD was appalled at the vast numbers of bottles of medicine which were, despite all checks, being supplied to the British public. When the increased cost of the pharmaceutical service was translated into terms of 210–220 million prescriptions a year one really had cause to pause On investigation relatively few drug prices had been found to be excessive Basically the increased cost was due to the fact that new and more expensive drugs were quickly replacing the old and traditional and cheaper brands. These new drugs were generally proprietary medicines, because a good deal of research was undertaken in the laboratories of manufacturing firms. Some was done in teaching hospitals and universities but at an early stage the researches had to be turned over to private manufacturing houses for development. A heavy research bill attached to most new drugs before they came on to the market and it was not unreasonable that these costs should find their way into the final cost of the medicine The percentage of prescriptions for proprietary drugs had risen he believed from 18% of all prescriptions in 1950 to 20% in 1954 Yet in other countries it was much higher and in France was probably about 80% These new drugs were saving money by making possible a more rapid turnover of hospital beds He was sure that substantial economies in the pharmaceutical costs in hospitals could be secured if the chief pharmacist in each hospital was a person of substantial scientific knowledge who was respected, and whose advice was listened to by the consultant and hospital medical staff We needed at the top a couple of dozen really first-class appointments that would encourage the intelligent young graduate to stay in hospital pharmacy and not go into industrial pharmacy

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[1] See *Lancet* Feb. 19 1955, p 400

In his reply Mr MACLEOD said that on the advice of the Public Accounts Committee they had last year embarked on a more realistic method of estimating which did not allow for possible increases in costs and wages If the general trend of prices was upward we must look forward to a series of supplementary estimates

Turning to the pharmaceutical services he said that the Ministry had completed their general investigation into the secondary manufacture and compounding of drugs and had stated a preliminary view that there was no evidence to show that excessive profits were being made. They were still considering the accountants' report on basic drugs There was a general downward tendency in the price of proprietary medicines, and he had no reason to suppose that the investigations were the reason for the reductions After the investigation was started the Association of British Pharmaceutical Industry had asked him to consider proposals which would alter the basis of the investigations He had agreed to do so, and that in part accounted for the delay The industry had made a wonderful advance in recent years, it had an important export trade, and research was vital to it He thought it right to proceed slowly, though the pace was slower than he would have liked But he was grateful for the coöperation of the industry and he was sure that it did not seek in any way to defend the indefensible

### CLINICAL RESEARCH

In the course of the debate Mr STEPHEN SWINGLER raised an important point of principle Experiments on human beings were, he agreed, necessary to increase medical knowledge, but doctors should be extremely careful not to use their privileged position to treat human beings merely as laboratory specimens Medical experiments on patients should not be conducted unless there was a chance of patients benefiting Clinical experiments in hospital should not be conducted unless the consent of the patients had been freely given in the knowledge of the nature of the experiments This principle was not being universally observed. In a recent case penicillin had been given to newborn babies, to observe their reaction and to establish the properties of the preparation There was no question of it having any beneficial effect on the babies It was established on inquiry that the consent of the parents was not sought, but, even if consent had been given, the experiment appeared to be ethically dubious and he wondered how far the consent of a parent to permit experiments on children was valid In the opinion of the Minister of Health, and those who conducted the experiment, there was no possibility of harm being done But in the issue of the *British Medical Journal* in which this experiment was published a doctor at a meeting of the Royal Society of Medicine was reported to have said that a physician should think twice before prescribing the first-ever dose of penicillin to any patient In the last two or three years at least half a dozen cases had been reported in the medical press of clinical experiments on children in hospitals, designed, not to benefit the children in any way, but to test the reaction of children to certain drugs That was treating children as guineapigs The Minister had said that judgment on this sort of question should be left to the clinician in charge of these cases, but some clinicians allowed their enthusiasm for science to override all moral considerations Mr Swingler urged the Minister to consult with his advisers and with the British Medical Association and the Medical Research Council, to see whether some kind of directive or code could be sent to hospitals to prevent and to prohibit experiments, especially on children, which were for purely scientific purposes, and were not designed in any way for the promotion of health

Mr JOHN RANKIN asked if Mr Swingler was aware that experiments were carried out on children not in hospitals One had been going on in an orphans Mr SWINGLER said he could only deal with He did not want to suggest that the practice was spread or that it had arisen from anything enthusiasm for science

Mr MACLEOD, in his reply, freely admitted th the example given the consent of the parents should been asked for The people responsible, who were pe of the very greatest authority and competence, regre as he did, that that was not done But he did not that it was wrong or unethical for any clinical in gation to be carried out which would not immed benefit the person on whom it was carried out. Wi clinical investigation and experiment our knowled medicine and surgery would not have changed ove centuries In his view, only the clinician in charge c say what was right and proper and what safeguards needed

It was not the Minister's duty—and he thoug would be wholly improper for him to try—to lay what ethical and medical principles should govern conduct of professional men If a small child of hi were in hospital and he was told by a professor of health "We are interested to know the effects perfectly safe clinical investigation It may very be that we can learn from what is done and as a r can drive still lower the infant-mortality rate in country," he would be more than ready to giv consent, he would be delighted Where a cli intended to undertake an investigation which w unusual and novel as to amount to an experime would be wise to seek consent from the patient or p but Mr Macleod was convinced that it would be w for a Minister of Health to issue directives on a m which was essentially one of medical ethics. SWINGLER interposed to ask whether the Minister not think that it was the duty and responsibility of heads of the medical profession to give some e guidance Would he ask the heads of the me profession to give some guidance?—Mr MAC found this suggestion more acceptable, and said th he had the slightest reason to believe that the p position was not fully understood he would info draw the attention of those concerned to what had said The Medical Research Council had sent c confidential memorandum rather on those lines. had no objection to what he might call an info notification from himself But he was clear th directive must come from the Ministry of Health matter of this delicacy

## Care of Spastic Children

Replying to a debate in the House of Commo Feb 14 on the welfare of spastic children, Mr D VOSPER, parliamentary secretary to the Minis Education, said that there were probably about 1 children under the age of 16 who suffered from disease About 3000 were under the age of five responsibility for their treatment was mainly th the Minister of Health, who was quite aware that t ment should start early Some 1500 were not cap of receiving education, even in a special school, and 3000 were very lightly handicapped and were in ordi schools Some others were in hospital or getting h tuition, and 1800 were in special schools

A survey of all physically handicapped children England and Wales, not only spastics, had lately b completed The Ministry now had the numbers, na and details of every child who, in the opinion of th local authority, required admission to a special sch The figure was approximately 450, of whom 400 requ admission to a boarding-school Mr Vosper admit that these children were not getting proper education the moment, but the schools for physically handica children already under construction would be more enough to cope with them In England 7 schools being built by voluntary bodies, and 3 by local author Some would be completed this year and, accor to the Ministry's plans, all would be completed 1058

Almost all the 3000 spastic children in ordinary sc were better off there, because they were receiving ent which they needed through the health service the remainder there was a difference of view as ether the children should be in special schools for es or in special schools for the physically handi d, as most were at the moment There was much said for widening the range of these children s ence and placing them among children with handi different from their own. The present trend was our of day schools rather than boarding-schools. important to keep these children with the normal as much as possible

Minister of Health and the Minister of Education agreed that where there was uncertainty, children not be classified as ineducable until there had trial period in a special school—even sometimes onged trial In conclusion, Mr Vosper emphasised alue of voluntary effort Here as in most social es, voluntary effort had done great pioneer work

### Civil Estimates

ording to the Vote on Account for 1955–56 which presented to Parliament on Feb 21, the Civil ates will be £2402 million compared with £2440 n last year Expenditure on the National Health ce is estimated at £463 million, an increase of million over last year

## QUESTION TIME

### Diacetylmorphine

Hugh Linstead asked the Home Secretary what action overnment proposed to take concerning the resolution ed by the Economic and Social Council of the United ns at its 18th session urging all governments to prohibit manufacture import, and export of diacetylmorphine t for such small amounts as may be necessary for ific purposes only —Major Gwilym Lloyd George d The Government have decided to give effect to esolution. Accordingly the current licences for the general facture of diacetylmorphine under the Dangerous Act, 1951 which expire on Dec 31 1955 will not be red After that date licences will only be granted for the facture of such small quantities as may be required for scientific purposes and for the production of nalorphine he manufacture of which diacetylmorphine is required intermediate stage Although the resolution makes no nce to nalorphine the discussions which led up to it nised that an exception for the manufacture of this drug d be required I propose to authorise no further exports drug save where the export is requested by a govern for one of these two purposes The import of diacetyl hine will not be permitted.

### Cadmium Poisoning

plying to a question Mr Harold Watkinson parlia tary secretary to the Ministry of Labour said that the sions in the Medical Research Council report on the d effects of cadmium poisoning in a factory at Prescot ashire were at present being studied on behalf of the rtment by the Chief Inspector of Factories. At the ories concerned measures which included improvements exhaust ventilation and closer medical supervision had ly been taken with the advice of the factory inspector to protect the workers against possible harmful concentrations admium fumes The effect of these precautions would inue to be carefully watched

plying to further questions Mr Watkinson said that y 14 such cases had been reported from 1938 to 1954 all the workers affected had recovered. But he was not g to minimise the importance of this matter There was doubt about the toxic nature of the fumes. The difficulty s to get an effective and reasonable cure Every effort uld be made to find such a cure as quickly as possible

### School Dentists

Replying to a question Mr D F Vosper, parliamentary tary to the Ministry of Education said that the equiva t of 979 full time dentists were working in the school dental ces in England and Wales on Dec 31 1954

### Military Hospitals

Replying to a question Mr Antony Head Secretary of te for War said that the proposals to spend £15 million r the next three years on building and modernising barracks uded the building and modernising of military hospitals As a start improvements at the Millbank and Cowglen military hospitals were planned

### Bequests of Bodies

Replying to a question Mr Iain Macleod said that the number of bodies received as a result of bequests under the Anatomy Act was 39 in 1944–45 and 157 in 1953–54

### Clinical Investigation

Mr John Rankin asked the Secretary of State for Scotland if he was aware that 600 children belonging to the Orphan Homes of Scotland, Bridge of Weir Renfrewshire had been used for the purpose of research into a new anti tuberculosis vaccine; that this experiment had been going on for the last three years and that now, as a result a number of the children were suffering from a chronic skin infection — Commander Galbraith replied In the course of vaccinating these children against tuberculosis it was arranged in the spring of 1951 between the Department of Health and the county council with the consent and coöperation of the management to use B C G vaccine for some of the children and the vole vaccine for others Earlier studies had suggested that vole vaccine was likely to give as good protection with less local reaction but late skin reactions on the site of the vaccination have been noted in 20 of 280 children who received this vaccine I am assured that these reactions have been slight and are all clearing up while the general health of the children has been entirely unaffected

### Private Nursing-homes

Replying to a question Mr Macleod said that at Dec 31 1953 the latest date for which information was available, the regional hospital boards which had contractual arrangements with profit making institutions which had remained outside the National Health Service and the average weekly charge paid for them by each board were as follows

| | | | |
|---|---|---|---|
| *General beds* | | | |
| South West Metropolitan | £8 | 19s | 8d |
| South Western | £13 | 13s | 0d. |
| *Maternity beds* | | | |
| Sheffield | £9 | 14s. | 5d. |
| South East Metropolitan | £7 | 18s | 8d |
| Oxford | £13 | 15s. | 4d |
| South Western | £14 | 14s | 0d. |

### Hearing-aids

Replying to a question Mr Macleod said that the numbers of hearing aids supplied to new patients in the four years 1951–54 were 56 997 87 925 85 093 and 67 534 In addition 36 457 66 519 96 726, and 116,878 aids were supplied in replacement of aids withdrawn for repair

### Mobile Radiography Units

Replying to a question Mr Macleod said that mobile radiography units had examined more than 3 million people last year The proportion of people examined who were found to have active tuberculosis showed a fairly steady decrease

## Cost of Drugs

The Minister of Health s reassuring words, in the debate on the supplementary estimates on the cost of drugs, are supported by a Treasury minute which appeared in a report from the Committee of Public Accounts.[1] The subject is of interest both to the Ministry and to the Treasury for about a third of the output of the pharmaceutical industry goes to the National Health Service. The Ministry s investigation into the cost of unbranded standard drugs and preparations which has lately been completed showed that, in a sample of nineteen companies with an annual turnover of about £24 million the annual average proportion of profit to capital employed was 13·0%. The Treasury agreed with the Ministry that this did not suggest that the level of prices in this field was excessive Investigations are still continuing into the price-level *of selected basic drugs and selected proprietary* preparations Principles on which it would be reasonable to fix prices for proprietary preparations are being discussed with the industry As an interim measure where it seems justified steps are being taken to see whether immediate reductions in prices can be secured Some firms have themselves already reduced the prices of particular proprietary preparations. The prices of some of the most widely used basic drugs, which have been falling for some years, have lately been further reduced

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[1] H M Stationery Office Pp 19 9d

# In England Now

*A Running Commentary by Peripatetic Correspondents*

THE smokeless age will not be without its difficulties With commendable self-sacrifice the inhabitants of the Palace of Westminster have abolished the last coal-fire from that ancient pile and it seems that the experiment is not proving an unqualified success No amount of hot air, no heated exchanges can compensate for the glow of self-satisfaction that used to beam on uplifted coat-tails An honourable and gallant member has complained to the Minister of Works that there is now no reasonable way for an honourable member arriving from the country in a chilled condition to thaw himself out other than by sitting on a radiator or having a hot bath The Parliamentary Secretary protested in vain that the central-heating plant maintained a temperature of 69° in the members' writing-room, and that an optional grilling to 75° could be obtained at the mere flick of an electric switch The beam had missed the target

The teaching of physiology is silent on the peculiar heat-absorption propensities of the human glutei I used to think it was a male phenomenon until I happened to catch my grandmother unawares with lifted petticoats before the drawing-room grate Perhaps that is something to do with ladies being so prone to chilblains, vasomotor control gets progressively inefficient towards the periphery There can be only one stance for the lords of creation on a cold day, the fires of inspiration kindle with spreading glow until the convection currents in the C S F swirl comfortingly around the hypothalamus

To essay the pose on a steam radiator is to invite the branding of a toast-rack pattern and the leaping alarm of a Texan steer To stand before an electric fire is to know the pungency of smouldering cloth against a scarlet calf The English way of life needs more than the forcing heat of American habit Long woollen underpants hide the gooseflesh beneath the pinstripe suiting No sitting around in the hall in armless singlets and cotton jeans for us While whole armies are sinking into the polar ice-cap in their pressurised tubes at 72°, we shall be chopping firewood from our last sledge to stand with all behind us in the southerly breeze

* * *

A complicated statistical survey at a secondary school in South Staffordshire suggests, from the size of the list, that almost every comic published, whether horrific or not, was read by someone in the school No doubt a few voracious readers can account for many of the least-read comics These are probably children whose parents bring "a pile of them home from work," as did the mother of one of the group of backward 10-year-olds whose essays on comics were exhibited Parental preoccupation with comics was illustrated by another essayist who said "you can't get a word in egewas when dad's reding comics"

The dangerous void of boredom which will be made by the withdrawal of horror comics will we hope be filled by periodicals from the 43 recommended by the National Union of Teachers as unlikely to have an adverse affect, on children and young persons Quickly scanning the list I was relieved to see that my children's comics were safely on it, so I shall still be able to follow week by week the fortunes of Dan Dare in his spacious battle of wits with the Mekon As one young essayist explained, it's the suspense of the weekly instalment that gets you

* * *

A brief introduction to Damon Runyan's American in *Guys and Dolls* before we left for the States convinced us that we would neither understand nor be understood Medicine being an international common footing we wondered whether we should revise our Latin, but in the excitement of departure Caesar, Virgil, and Ovid could not easily be found We would perhaps have been wiser to have bought an Anglo-American dictionary, and this might well be included in the instruction list supplied to Fulbright scholars and others visiting the New World With no such enlightenment we stumbled along the language path, at times surprised by the paucity of dialects in a country so large and a little homesick for the broader accents Now we no longer call our chocol anything but candy and successfully contort our m to reverse the dates on letters But often we won how the garage hand at home will take to our orders f gas or the repair of the hole in our muffler We w relieved to find malapropisms exist and were deligh to hear of the Cushing patient who had not been weig in pounds, or even the unheard-of stones, but kilowatts

* * *

I was surprised to see on the ward sister's medi list the *array of non-specific stock mixtures*— expect stim, mist rhei co, and so on—that have s how accumulated against the names of the longer patients Specific drug therapy is watched carefully, a course of this usually ends when a given total am has been taken, or when its ineffectiveness has be apparent But it seems easier to order a non-spe mixture than to stop it For one thing, the reasons prescribing it may be obvious, but the reasons for continuing it are less striking Again the mixture have been prescribed originally by the H P, the regis or some other member of the staff, and it may been ordered by telephone, not written in the notes, then forgotten by the prescriber In one military ho the ward medicine list went by bed numbers instead by patients' names, and by cumulative action a patient might find himself receiving mixtures presc for one or more of his predecessors in the bed

* * *

The cost of the National Health Service has made people money conscious, often people whom you would expect, and my examiner, an eminent physician h accounts, was by way of being something of an econ

"How would you perform Benedict's test?" he asked rather as you would throw a dog a bone

"Well, sir, I'd pour urine into a test tube to the dep one inch and add eight drops of Benedict's re "

"You'd do what?" he screamed

"I mean, sir, that I'd pour Benedict's reagent into a tube to one inch deep and add eight drops of urine," I corr myself

"Tell me," he said, "would the test work if you used an inch of Benedict's and four drops of urine?" He sat in his chair and eyed me beneath his large, bushy eyeb

"Well, er, sir, I suppose it would," I replied doubtf It seemed logical, but these half quantities never seem appear in the textbooks

"It most certainly would, young man!" he cried, lea forward and fixing me with a stare, "and save the cou £50,000 a year!"

* * *

"Thirteen dormies are full up—also we've got measle mumps which I've luckily had, they keep us in bed for here, five days he says at the *least anyway* two days your temp is normal which mine isn't yet They s me with Bovril and dry bread which is awfully mean others in my dormy have normal temps and have baked b and jelly"

Such is flu at school Starve a fever and give a g dose of salts How long is it since starvation diet typhoid took its toll of exhaustion and death, and water-only régime after a hæmatemesis led to hunger wasting? It takes more than a friendly suggestion f authority to convince a confirmed school matron th food, if it is wanted by the patient, is usually good her, and that nice things are not of necessity al harmful

* * *

*More News from School*—"As you probably deduced fro slight Sunday letter deficiency, I have had 'flu I thou I had escaped it until Wednesday morning, when I secret took my temperature and registered 99$^1/_2$° *After* the ... house match, that afternoon (3–3), for some reason I did feel a *lot* better, so I told the correct authorities. Overwo you'll feel better tomorrow' Tomorrow, as it happen felt no better at all, and the next day *rather* worse than On Saturday I registered 102$^1/_2$°, felt so dizzy that I dr the thermometer (4*s* 6*d*) and began to think it was get beyond a joke Since then I have been here, suffe 'Flu does seem to be good for Latin though, for last w prose I got α. Enough of disease Thank you excee much for the cake"

# Letters to the Editor

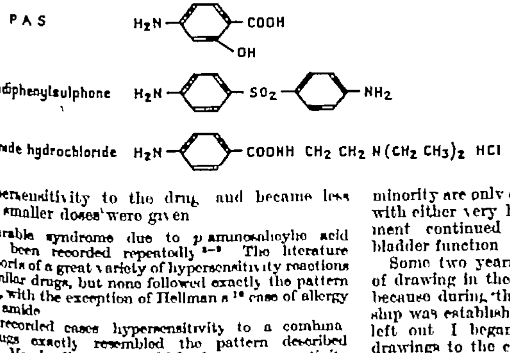
## CAPITAL PUNISHMENT

ir,—In the account in your last issue of the debate in liament on capital punishment, I read that the rney General reiterated the Government's view with the *rising figures for crimes of violence* we ld not risk at this time abolishing or suspending the th penalty" I am quite unable to understand this ument It would make sense only if it were generally pted that capital punishment were the best deter , but this is the very point in dispute It is open s opponents to say that *because* crimes of violence ising capital punishment has failed of its purpose ppose that in fact these crimes were lessening ht not Sir Reginald then have argued that there was oint in suspension or abolition because the present em was working very well ? It seems to me that no ter which way the figures for crime are moving the onents of change could use them to bolster up their

ndon, N W 1        E. HINDEN

## PERSENSITIVITY TO PRIMARY AROMATIC AMINES

r,—In 1950 we observed[1] that in African patients leprosy treated with diaminodiphenylsulphone yndrome sometimes developed closely resembling dular fever, and characterised by fever lymphadeno y generalised dermatitis mononucleosis albuminuria in severe cases, jaundice When first noted by [1] this syndrome was taken to be glandular fever asked by the drug, and, moreover the Paul Bunnell was positive but later it became apparent that it a hypersensitivity to the drug and became less mon if smaller doses were given



comparable syndrome due to *p* aminosalicylic acid s.) has been recorded repeatedly[2-9] The literature ains reports of a great variety of hypersensitivity reactions any similar drugs, but none followed exactly the pattern r cases, with the exception of Hellman's[10] case of allergy rocaine amide

n some recorded cases hypersensitivity to a combination of drugs exactly resembled the pattern described re (e.g., Marsh's[11] case in which there was sensitivity s., streptomycin, penicillin chloramphenicol and local esthetic). The patient noted by Jeffrey et al[12] became itive to P.A.S., streptomycin and penicillin and they rred to another patient who initially became sensitive to s, and subsequently reacted violently to streptomycin cillin, and Sulphatriad' Since P.A.S is a common ominator in all these cases, P.A.S is probably the mary sensitising agent Hill[13] discussing Marsh's case says When one patient shows hypersensitivity to several drugs it is hard to decide whether one is dealing with a mixture of specific reactions or whether there is a true 'cross reaction Accordingly one wonders whether there is anything common to the chemical structure of P.A.S diaminodiphenylsulphone and procaine amide or to their breakdown products that might account for their causing the same hypersensitivity reaction Their formulæ indicate that all are primary aromatic amines these compounds are thought by Hill to be allergenic while Marsh suggests that the *m* aminophenol produced during their breakdown, may be responsible In either event it is puzzling why the syndrome is not seen with sulphonamides *p* aminobenzoic acid or procaine compounds, since all these contain primary aromatic amines.

Bowie[14] suggests that sensitisation by a previous infection is required for a syndrome of lymphadenopathy mononucleosis and heterophil antibody production, and that the trigger action is provided by subsequent reinfection with the same, or closely allied, organisms. In many cases the agent is probably the organism responsible for epidemic glandular fever, but viruses bacteria or even protozoa may possibly produce similar results in sensitised persons We now suggest that certain drugs containing primary aromatic amines may also produce the syndrome

JOSEPH BARNES
Dublin        ELIZABETH J BARNES

## TREATMENT OF ENURESIS

SIR —Your leading article of Feb 19 was most valuable but you stress the physical factors more than experience with children seems to warrant As you rightly point out the presence of an accessory valve is no evidence that it is the cause of dysfunction

In my clinic for enuretics, where during the past four years over 100 patients have attended microscopical investigation of the urine was discontinued, because of the persistently negative results There are however some other facts which appear significant though a full analysis of the case histories has not yet been possible The most common single factor is the birth of a sibling before the enuretic to be was 2¹/₂–3 years old The gap between the siblings is often much less. *In some others a major illness* or separation occurred between the age 1¹/₂ and 2¹/₂ The remaining minority are only children where a very powerful mother with either very high standards or considerable resentment continued to focus the child's attention on his bladder function

Some two years ago having realised the significance of drawing in the analytical treatment of children and because during the history taking inevitably a relationship was established with the mother and the child felt left out I began asking the children to bring their drawings to the clinic These drawings provide a most interesting clue to their fantasy life While looking at these drawings the mother's physical presence could be disregarded for several reasons The child and the doctor were together occupied in looking at the pictures the child offering his explanations and the doctor offering comments which responded to the fantasy context and which the child understood, *but the mother did not* This has saved much time and it has also established a very personal relationship between the child and the doctor

Some of these drawings are worth mention.

A girl of 9 who had 3 sisters and was always helpful obedient submissive and undemanding brought a drawing representing a female figure There was a large hat decorated with flowers no face or upper part of the body but a very large abdomen, which she called an apron This thinly disguised tummy was decorated with pockets which were babies' heads This gave a clue how great her preoccupation was with the number of children who appeared and that this anxiety found outlet in her nail biting and enuresis We were able to talk about these "pockets" and both understood what they meant, and she could give a fantasy life to them, which closely corresponded to her real feelings about her sisters

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[1] llay E. J., Barnes, J *Lancet* 1951 ii 905
[2] Lowe J., Smith, M *Int J Leprosy* 1949 17 181
[3] thbert J *Lancet* 1950 ii 209
[4] rstad O *Tidsskr norske Lægeforen* 1951 71 753
[5] B *Tubercle, Lond* 1953 34 23
[6] McKendrick G D W *Lancet*, 1951, ii 668
[7] owland D *Tubercle Lond.* 1953 34, 143
[8] Franke P *Ned. Tijdschr Geneesk* 1952 96 2001
[9] h, K J *Brit med J* 1952 1 416
[10] Hellman, E. J *Amer med. Ass* 1952 149 1393
[11] Marsh, K *Lancet* 1952, ii 606.
[12] Jeffrey B. Borrie P., Macdonald N *Brit med J* 195[illegible] ii [illegible]
[13] Hill J. R *Lancet* 1951 i 900

[14] Bowie J C *Brit. med J* 1951 i 923

A boy of 6, who had had a very disturbed early childhood, especially after his first year, had continuous dribbling of urine Enuresis was less frequent He was an only child The mother was a very masculine type and her maternal feelings were very mixed In some ways she could be a good mother, especially where the boy's physical welfare was concerned, but in other ways she had to reject him The relationship reached a stage, by the time they came to the clinic, where her rejection was continually justified and reinforced by the soiling of household articles and the boy himself was involved in a "total" defence By this I mean that he was physically hyperkinetic, unable to relax, emotional restlessness made him talk ceaselessly and he dribbled urine The mother brought typewritten sheets with her, which described the events of the day, with particular emphasis on what has been ruined The drawings the boy brought were copious, but every one of them represented a peak Tents, houses, aeroplanes were all made in the shape of a cone and he had apparently repeated this pattern endlessly It was impossible to explain to the mother that the boy's whole behaviour was a desperate attempt to reassure himself through his masculinity, but one could talk with the boy about the power, goodness, and effectiveness of these peaks Reassurance was conveyed through these hypothetical objects and he was able to respond by less dribbling This easing of the symptoms and the appreciation her boy found in the eyes of someone else, enabled the mother to be less rejecting

Another boy, aged 8, who had an elder and a younger sister, the younger having been born when he was 1½ and just recovered from an illness, brought drawings of a toy town While explaining who were represented in the drawing, he suddenly remarked "Gillian is not there" Gillian being the younger sister and very much a thorn in his flesh, and one to whom he could never in reality stand up, this was an excellent *opportunity to present a world without Gillian* The masses of smoke coming out of chimneys, a car labouring almost perpendicularly uphill, were all representative of his efforts to combat the world with Gillian, nevertheless In other words, although he created a world without his sister, in this one he still continued to behave as if she was there The duality of his emotions was appreciated and his attempts to cope reinforced His enuresis stopped after four months

It seems to me that the enuretic child would benefit less from extensive investigations than from understanding what his enuresis stands for in his fantasy For a submissive child it may represent the only socially acceptable form of revolt, since nowadays all parents know that enuresis is not conscious wickedness, it may also represent one aspect of an over all aggressiveness, which in turn comes from insecurity It might be interesting to find out whether the time of the arrival of other siblings plays as great a part in the establishment of enuresis as our case-histories seem to suggest It would also be interesting to know whether major trauma at this period acts through regression, or through lack of security at a period when toilet training is usually completed

London S W 15 HEDY SYMONDS

SIR,—"*We are not so well equipped to treat enuresis that we can ignore any promising technique*" Your interesting leading article makes this valuable point

In pursuit of this ambition it is worth while quoting Braithwaite's work with enuresis[1] He described 21 children treated by hypnosis Only 5 were unaffected and the remainder were improved He found that direct suggestion used under hypnosis, was of more value than any other method I treated 40 cases with similar results[2] As long ago as 1887 Liebeault[3] published the results of 77 cases treated for enuresis; only 8 showed no improvement Cullerre[4] reported 24 cases with 21 recoveries, Bramwell[5] described 18 cases of which recovered, and there were no relapses after some ye Wyllie[6] has reported that "obstinate cases of enures responded to a concentrated form of suggestion, nam hypnosis"

There seems little doubt that hypnosis destroys the an invariably associated with the act of wetting the bed. majority of cured enuretics will maintain that a wet followed the thought "I might wet my bed" W children, following suggestion, with or without hypnosis, stated "I don't seem to worry any more, even if I we bed I won't worry" This statement has been confirme other workers[7] It is, of course, the suggestive element puzzling condition that makes assessment of drug treat (or any other treatment for that matter) so difficult due consideration of your leading article, it seems worth to follow up this line of treatment with controlled re

London W 1 GORDON AMBROS

## GENITO-URINARY TUBERCULOSIS

SIR,—In answer to Dr Haines's letter of Jan I should like to quote the following figures from Wr ington Hospital Wrightington Hospital is a sanato which largely treats non pulmonary surgical tuberc and these figures are for the last three years D this time the total number of all female cases disch was 486, and of this number only 26 had gynæcol tuberculosis None of these 26 had a concomitant lesion Since 1952, 40 female cases of tuberculosis renal tract have been treated in the genito u unit, and only 4 of these have had a co existing gy logical lesion It should be pointed out, however, routine urine examinations are not carried out on genito urinary patients unless they complain of symp related to the renal tract It is therefore possible tha or two cases may have been missed, but even would not alter the findings in this unit that in female it is uncommon to find genital and renal l occurring together

Liverpool J G Go

## PSYCHOLOGICAL ASPECTS OF UTERINE DYSFUNCTION

SIR,—Dr Cramond in his article (Dec 18) conc that "fear, emotion, and anxiety play no part in outcome of labour from the practical obstetrical po view—i e, in determining the length of labour or wh forceps will be necessary"

The article, which is concerned with inertia, m no study of the indications for the employment of f and the second part of the conclusion is thus entirely un

The first part of Dr Cramond's conclusion—dealing the length of labour—is based on an analysis of factor as home environment, the mother's or sisters' ob history, psychosexual adjustment and dreams and an in pregnancy Other factors which may be relevant, s whether the pregnancy was planned or not, the leng marriage before conception, relative fertility, and pre abortions are neglected In addition the puerperium, emotional tensions are notoriously heightened in women, may be an unsuitable time for accurate psycho assessment

Certain factors make those who study women *labour rather than in the puerperium* feel sure their fears and anxieties play a considerable part influencing the course and duration of their labour

1 The greater frequency of inertia in strange hosp surroundings, as opposed to domiciliary practice

2 The frequency with which contractions in early la cease for a while when a patient is first admitted to ho with its strange atmosphere and perhaps the compa other—distressed—patients

3 The greater frequency of postpartum hæmorrh hospital practice

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[1] Braithwaite, J V C *Practitioner* 1950 165 273

[2] Ambrose G, *In* Hypnosis in Modern Medicine Oxford, 1953 p 106

[3] Liébeault A A *Rev Hypnot Paris* 1887 1 71

[4] Cullerre A *Z Hypnot* 1891, 4 377

[5] Bramwell J M Hypnotism London 1930, p 23

[6] Wyllie W G A Survey of *Child Psychiatry* Oxford 1 p 207

[7] Newbold G Handbook of Medical Hypnosis London published shortly

The very real effect of what is glibly called sedation reassurance but which may make all the difference he course of a woman s labour and her outlook on future nancies.

hese facts are mentioned, not in advocacy of more ensive domiciliary practice but to emphasise the essity for "psychological' preparation in the natal period

n a study on the human uterus in labour Garrett[1] demonstrated one possible way in which inco nate uterine action may be produced by maladjust t between the amount of adrenaline and noradrenaline ased at sympathetic nerve endings in the uterus

he recognition of the importance of the mother s tal outlook is an important part of antenatal and natal care, with its resultant decrease in maternal fetal morbidity , and any rash disparagement of —possibly based on insufficient evidence—would ar to be a step in the wrong direction

don, N.W.3 H E REISS

## TIFICIAL HIBERNATION IN POLIOMYELITIS

R,—Dr Haeger and his colleagues (Feb 19) and Brehme (Jan 15) advocate the use of artificial nation in the acute stage of poliomyelitis I think ever, that such experiments are not justified until matter has been investigated experimentally in als During the acute stage of poliomyelitis the fate ns of thousands of motor cells hangs in the balance this is not a situation in which experiments on ents with new drugs is justifiable Factors which ence the virus-cell relationship at this critical stage being much studied by virologists and it is to be ed that the effects of artificial hibernation if any be elucidated by them

partment of Neurology
ited Oxford Hospitals W RITCHIE RUSSELL

## PERFORATED PEPTIC ULCERS

R,—I was most interested in Mr Moore s compre sive review of 125 cases of perforated peptic ulcer our issue of Jan 22, and also in Mr Grieve's letter b 5

n Mr Moore's series of 66 cases treated conserva ly 5 were unproven (table I) and should be dis ed and another patient who died and was treated ervatively and unaccountably included in the simple ure series (table II) should be added If these changes allowed, the mortality for Mr Moore s conservatively ated cases is 6 6% whereas his mortality for simple ure is 2 2% This suggests simple suture is preferable pite of its apparent higher morbidity in Mr Moore s es

nlike Mr Grieve I support Mr Moore s contention t conservative treatment is nearly always fatal in the rely ill and shocked patient. As Mr Moore states se patients must be resuscitated rapidly and operated n. The ill patient is often elderly and the diagnosis ertain (note Mr Moore s case of strangulated jejunum nosed as a perforated peptic ulcer) and X-ray amination would be an added burden to these ill ients I have stressed this point elsewhere[2] I must agree however with Mr Grieve s criticism f table V which appears too diffuse to be of any real atistical value

Mr Moore s radiological technique is ingenious and ay well be useful but it does not appear to be uniformly essful in all cases This stimulating paper gives ther food for thought about a very common surgical dition.

n Hospital,
Manchester N F KIRKMAN

## MENTAL HEALTH AND PUBLIC HEALTH

SIR —May I, as the editor of the London County Council study group s report[1] comment briefly on the points raised by Dr Small and Dr Ring (Feb 19) ?

To say that it is impracticable to introduce preventive mental health work into the public health service at present because the service is completely unrepresentative of the public as a whole ' is I think, a little too sweeping Coöperation between family doctor and the public health service is growing all over the country, a trend which has been happily underwritten by recent B.M.A policy[2] Nowadays public health doctors and health visitors are tackling their work more and more against the background of the family as a unit rather than by considering the problems of the individual in isolation It is true of course that we have a long way to *go yet*—shortage of health visitors is one of the factors holding up more rapid progress—but the service is undoubtedly reorientating itself and offers increasing opportunities for preventive mental health work with the great advantage of the normal setting in which we are privileged to operate

Dr Ring stresses the need for more adequate mental health training of public health workers Most of the L.C.C study group s report concerns itself with this very problem the need for better training in mental health is part of the D.P.H D.C.H and health visitor courses is recognised but beyond this emphasis is laid on intensive in service training schemes of existing public health staff

We considered it essential that such training should be undertaken on an entirely voluntary basis, and advocated that it should take the form of regular case conference discussions between child welfare and child guidance teams operating in the same area Some pilot groups are already in existence to draw definite conclusions from their experience would be premature but the insight into mental health problems which doctors and health visitors are gaining is being generally welcomed and contributes greatly to the interest and value of their daily work.

Divisional Health Office
Wandsworth
London S.W 18 WILFRID G HARDING

SIR,—A London County Council study group (consisting of public health medical officers, psychiatrists health visitors and a psychiatric social worker) reporting on the rôle of local health authorities in mental health gave particular credit to the work being done by recently trained health visitors and expressed regret that the D P H course did not as yet give sufficient space to mental health The Society of Medical Officers of Health in its recent memorandum on the future of child welfare centres gave pride of place to work on mental and emotional problems. The Minister of Health and the Secretary of State for Scotland in circulars issued at the end of 1954 reminded local health authorities that the work of the health visitor now extends to cover the whole field of prevention of ill health including prevention of mental ill health

Challenging these weighty authorities Dr Cameron (Jan 29) asserts without offering any supporting evidence that a health visitor is by her general nursing training quite unsuited for mental health work that her further training does little to equip her to enter this field, and that a better person would be an unspecialised social worker

May I ask him two questions ? Does he similarly consider that a background of general medical training completely unfits a doctor for all varieties of preventive work and if so will he resign his lectureship in favour of a non medical social worker ? Is he aware of the

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1 Garrett W J *J Obstet Gynæc Brit Emp.* 1954 61 586
Kirkman, N F *Postgrad med J* 1955 31 [illegible]

1 *Med Offr* 1954, 92, 303
2 *Brit med J* 1954 i suppl p 12

very large amount of time devoted in the health visitor's training to the psychology of development and allied subjects ?

As an individual taking part in the teaching both of D P H students and of health-visitor students, I can assure your readers that the London finding is not restricted to the Metropolis We can equip public-health doctors more adequately for mental health work by improving their training, not by attacking other people who are already doing excellent work

Health and Welfare Department,
Corporation of the City
of Aberdeen

I A G MACQUEEN

## EPIDEMIC VERTIGO

SIR,—After Dr Leishman's article of Jan 29, I thought your readers might be interested in an outbreak that I have seen here in the last few months, and in its interesting sequel

Between Oct 31 and Jan 31 I saw 6 mild cases of this disease, all within two miles of each other, and none with any social contact The ages of the patients were between 45 and 70 2 of them fell ill on the same day

In all cases the onset was acute , the patients woke up with intense vertigo, followed by vomiting There was no nystagmus or ocular palsy They all had intense photophobia They were kept in bed for 7–10 days and given phenobarbitone (gr 1 b d ) and mist bismuth fort (t d s ) They were able to return to work in three weeks, quite normal

I have seen in the last twenty years several other similar cases which have followed the same pattern and have had no after effects

There is little pathological evidence about these cases, but, thanks to Dr W M R Henderson, of Pembury Hospital, I can give what I think is some valuable though negative evidence

One of the 6 patients, a man aged 68, died suddenly while riding his bicycle in Tonbridge He was taken to Pembury Hospital, where a post mortem examination established that the cause of death was coronary thrombosis Serial sections of the inner ears revealed nothing abnormal at all, eight weeks after the attack of vertigo I realise that this is negative evidence but it may contribute something to our knowledge of this little known but very disabling disease I think the mid brain is the next place to look for abnormal findings

Hadlow Kent

JOHN B MARSHALL

## LIFE-ASSURANCE UNDERWRITING

SIR,—Your annotation [1] on this subject includes certain remarks which, I feel, cannot be allowed to pass without *comment In the assessment of risks three methods are* available

1 There is the method of adding to the proposer's actual age the number of years estimated to compensate for his reduced expectation of life, and to charge the higher premium applicable This method is suitable for the increasing type of risk—for example, obesity or hypertension—provided the additional premium is not too heavy

2 The second method is to impose a diminishing lien whereby a proportion of a capital sum is deducted in the event of early death The deduction is reduced yearly, so the proposer obtains the full cover on attaining the agreed age This method is suitable for the decreasing type of risk—for example, recent pleurisy or peptic ulcer—and it is very often invoked when by the first method the additional premium would be too high The disadvantage of this method is that it does not provide adequate cover for dependents or for collateral security

3 The third method, which is commonly used in the U S A and is now finding favour in Pakistan, is the numerical method, whereby the risk is assessed under various headings, such as build, personal history, family history, occupation, certain confidential information, and physical condition This method is of value in assessing both the increasing and the decreasing types of risk, at the same time providing a full cover from the inception of the policy The numerical method is based on a vast compilation of statistics

*You remark that recent advances in medicine* had little or no impact on life assurance practice. by the numerical method every recent advance influe the assessment of a risk

For instance, a person who has had spontaneous pne thorax, if thought to be non tuberculous, can be acce without loading , and so, too can one who has had ple if this is judged to be non tuberculous and the person is average weight The greatest change, of course, has bee those diseases which are amenable to antibiotic the In Pakistan patients with malaria can be accepted a ordinary rate , and the applicant with a history of a acute attack of amoebic dysentery treated with antiamoeb drugs can also be accepted without loading

The outlook in life assurance underwriting is not so as you make it seem By the numerical system of u writing, and a wide search for statistics of life underwriting can be made scientific In this specialisation, life assurance medicine is in danger becoming a speciality on its own Yet this work o opportunities to the general practitioner for re of the sort suggested by the College of General Pr tioners It is the surest means of studying what the Prof J A Ryle called the " natural history of dis

R B F KHAMBATTA

Medical Director for Pakistan American L
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Karachi

## CORTICOTROPHIN GEL AS A TEST OF ADRE CORTICAL FUNCTION

SIR,—In your issue of Nov 27 Dr Nabarro desc a procedure for assessing adrenal function In spit its apparent completeness this test may occasion *give rise to incorrect results, as is shown in the follo* case, which is also a further example of recovery Waterhouse Friderichsen syndrome treated with c sone [1]

On Nov 22, 1954, a boy of 4 was admitted to this hos with a twenty hours' history of abdominal pain, head and vomiting , there was marked neck retraction, a pur rash over the lower half of the abdomen and scrotum, an imperceptible pulse, with the blood pressure systolic 50 Hg, diastolic unobtainable

*Laboratory Findings* —White blood cells 19,000 per c (83% neutrophils) Cerebrospinal fluid was macroscop clear with 25 white cells per c.mm Cerebrospinal fluid blood culture *Neisseria meningitidis* grown

*Treatment* —Penicillin 20,000 units was given intrathe (one dose), and 250,000 units intramuscularly, six hourly six days , and cortisone 25 mg intramuscularly six-ho for three days, reducing gradually over the next three

The patient's condition improved gradually Three after admission the blood pressure was 80 mm systolic, two days later it gradually rose to 90/60 On disch thirty one days later, it was 90/55 Prior to discharge serum potassium was 4 6 m eq and sodium 129 m.eq per l

In view of the low serum sodium the child was readmit one month later for assessment of adrenal cortical functi The test was performed as described by Dr Nabarro Cort trophin (A C T H ) gel 25 units was used as the stimulat dose in view of the child's age The 17 ketogenic ste output was estimated in addition by the method of Norym berski et al [2] adapted for use with ether as solvent Th results were as follows

| | *Eosinophils (per c mm )* | *Na/K ratio* | *17 ketosteroids (mg per 24 hours)* | *17-keto steroids (m per 24 hou* |
|---|---|---|---|---|
| *Before corticotrophin* | | | | |
| Day 1 | | 2 6 | 0 6 | 1 3 |
| Day 2 | 64 | 1 4 | 0 4 | 1 3 |
| *After corticotrophin* | | | | |
| Day 3 | 68 | 1 0 | 0 6 | 2 0 |
| Day 4 | 87 | 2 0 | 0 5 | 2 3 |
| Day 5 | 61 | 2 7 | 0 6 | 3 5 |
| Day 6 | 24 | | | |

It will be noted that none of the criteria of norm function as laid down by Nabarro are satisfied, yet th

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1 *Lancet* 1954 ii, 1168

1 Buzzard, E M Higgins G Newborne L P A, Race J *Lancet* 1953, ii 907

2 Norymberski J K, Stubbs R D, West, H F *Ibid,* 1 i 1276

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h Green Hospital,
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HUGH R E WALLIS

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R,—I was very interested in the paper by Dr rman and Professor McCance in your issue of 12. Their patient had an acidosis with low serum ssium and she developed tetany during the treat nt with potassium salts when the serum-calcium was mal and the $CO_2$-combining power still low May er an explanation for this rather puzzling phenome , which I believe is in agreement with the authors ral idea?

n 1928[1] I reported investigations on the influence arious ions on the galvanic excitability of peripheral ves in latent infantile tetany It was found that the on of cations and anions corresponds closely to position of these ions in the Hofmeister-series in the m of physiological hydrogen ion concentration

his series, which was obtained by the study of colloid otic swelling of gelatin in salt solutions shows changes may be even inverse with a change of pH, but near to the ysiological hydrogen ion concentration it is as follows cations, $Li<Na<K<Rb<Mg<Ca<Sr<Ba$; and for ons citrate<tartrate<$HPO_4$<$CH_3COO$<Cl<$NO_3$<Br CNS. Cations and anions both show a water retaining ect on the left side while the repelling of water increases ards the right side

It is interesting that the patient of Dr Fourman and essor McCance developed œdema at the time of tetany n the experiment the action on electrical excitability was ry similar to that on water retention Calcium and mag esium decrease the excitability potassium increases it he action of sodium is demonstrable only when given ether with another water-attracting ion, particularly as trate The effect of citrate should be the same but it s clearly demonstrable possibly because of its trans mation into isocitrate and its incorporation into the carboxylic cycle In sodium chloride the effect of the ion appears to be over-compensated by that of the anion rticularly striking is the synergism of calcium and magnesium ions when compared with the specific antagonistic action on the brain[2] and on the pressor effect of adrenaline[3]

In the case described the treatment did not result in abnormally high potassium levels but the increased renal potassium clearance suggests an analogous alteration of the blood tissue barrier and makes it probable that the rapid change from hypopotassæmia resulted in an ionic imbalance within the tissues, and correspondingly to an increase of the excitability of peripheral nerves or neuromuscular junctions It is in agreement with the mentioned rôle of ions that both potassium and sodium citrate aggravated the tetany

Pathology Department
Children's Hospital, Birmingham.

H S BAAR.

## MANIPULATION AND CERVICAL SPONDYLITIS

SIR,—Mr Stamm has hit the nail on the head in his letter of Feb 12 Pathological conditions involving the cervical spine pass through phases sometimes acute, subacute, or chronic and according to the symptoms they produce the patients are often seen by different types of doctors and often require different types of treatment for whatever phase they happen to be in I would agree with Mr Stamm on the beneficial effects of a controlled manipulation under thiopentone in the stage of which he speaks

It has been shown that pain in the neck, apart from disc degeneration and herniation is often caused by root-cuff fibrosis[4] and osteo-arthritis of the joints of Luschka.[5]

In the early acute or subacute phases we often give gentle manipulative stretching without an anæsthetic combined with support of varying degrees, physiotherapy medicinal treatment and local injections into tender points, according to the type and severity of the case If the aggravation by treatment is sharp we may stop it and substitute rest support, warmth and sedation. We give treatment in the acute and subacute phases and observe its effect and the tissue reaction. If there is an aggravation we call this "purposeful aggravation" since it gives us a lead as to the course the condition is taking Many cases thus treated quickly become symptom free

After a series of progressive gentle manipulations we feel that a condition may develop which would coincide with that described by Stamm, when a controlled manipulation under thiopentone gives more lasting results as terminal adhesions are freed

We realise that there may be many factors in the production of disc degeneration such as the stress syndrome the presence of septic foci, toxic allergic conditions, and possibly diet which may have an effect on the water content of the disc. Is it not true that postural and occupational strains are also a most important factor and often account for the involvement of the muscles?

We believe that there is a condition of chronic postural strain affecting in the neck and shoulder-girdle region, the posterior cervical muscles including the trapezius, the levator anguli scapulæ and the rhomboids as well as the scapula fixing serrati. Unless the head and shoulders are held correctly these muscles are strained and become tender

So many authorities are against the use of the term "fibrositis because they argue that the condition cannot be proved morphologically Bruce Casselman the histologist in a personal letter states: Ideally histochemical studies are correlated with studies of function so that a comprehensive investigation has three dimensions function chemical composition and structure Depending upon the pathogenesis of the condition it is frequently possible to detect alterations in the first two before there is any change in structure that would be revealed by the conventional histopathological methods.

Is it not possible that these tender points in muscles are due to chemical changes first and not to cellular ones? If we think carefully it is clear that they occur chiefly or almost entirely in the anti gravity muscles.

Other physical signs and symptoms often change with the degree of muscle tenderness. Later because the muscles are not supporting the joints these become strained and some or very large amount of time devoted in the health visitor's *training to the psychology of development and allied* subjects ?

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[1] Baar H. Mitt Ges inn Med. Wien 1931 23 9 Z Kinderheilk. 1915 46 102.

[2] Meltzer S J., Auer J Amer J Physiol 1905 14 366 Ibid 1906 16 233

[3] Baar H J exp exp Med 1946 50 591

[4] Brain W R. Lancet 1954, i 497

[5] Cave A J E., Griffiths J D., Whiteley M M. Ibid Jan. 22 1955 p 176

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## MANIPULATION AND CERVICAL SPONDYLITIS

SIR —Mr Stamm has hit the nail on the head in his letter of Feb 12 Pathological conditions involving the cervical spine pass through phases sometimes acute, subacute or chronic and according to the symptoms they produce the patients are *often seen by different types of doctors* and *often require different types of treatment for whatever phase they happen to be in* I would agree with Mr Stamm on the beneficial effects of a controlled manipulation under thiopentone in the stage of which he speaks

It has been shown that pain in the neck apart from disc degeneration and herniation is often caused by root-cuff fibrosis[4] and osteo arthritis of the joints of Luschka[5]

In the early acute or subacute phases we often give gentle manipulative stretching without an anæsthetic combined with support of varying degrees, physiotherapy medicinal treatment and local injections into tender points according to the type and severity of the case If the aggravation by treatment is sharp we may stop it and substitute rest support warmth and sedation. We give treatment in the acute and subacute phases and observe its effect and the tissue reaction. If there is an aggravation we call this purposeful aggravation since it gives us a lead as to the course the condition is taking Many cases thus treated quickly become symptom free

After a series of progressive gentle manipulations we feel that a condition may develop which would coincide with that described by Stamm when a *controlled manipulation under thiopentone* gives more lasting results as terminal adhesions are freed

We realise that there may be many factors in the production of disc degeneration, such as the stress syndrome the presence of septic foci, toxic allergic conditions and possibly diet which may have an effect on the water content of the disc. Is it not true that postural and occupational strains are also a most important factor and often account for the involvement of the muscles?

We believe that there is a condition of chronic postural strain affecting in the neck and shoulder-girdle region the posterior cervical muscles including the trapezius, the levator anguli scapulæ and the rhomboids, as well as the scapula fixing serrati. Unless the head and shoulders are held correctly these muscles are strained and become tender

So many authorities are against the use of the term "fibrositis because they argue that the condition cannot be proved morphologically Bruce Casselman the histologist in a personal letter states: Ideally histochemical studies are correlated with studies of function so that a comprehensive *investigation* has three *dimensions*: *function chemical* composition and structure Depending upon the pathogenesis of the condition it is frequently possible to detect alterations in the first two before there is any change in structure that would be revealed by the conventional histopathological method "

Is it not possible that these tender points in muscles are due to chemical changes first and not to cellular ones? If we think carefully it is clear that they occur chiefly or almost entirely in the anti gravity muscles

Other physical signs and symptoms often change with the degree of muscle tenderness Later because the muscles are not supporting the joints these become strained and some or all of the muscles of the cervical joints go into protective spasm Thus the muscles of an area are affected (1) in the early stages by postural strain , (2) later when they go into spasm as a protective phenomenon , and (3) by a true fibrotic state associated eventually with spondylosis Local injections in any stage will often produce benefit

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[1] Baar H *Mitt. Ges inn Med Wien* 1924 23 0 *Z Kinderheilk.* 1928 46 602

[2] Meltzer S J., Auer J *Amer J Physiol* 1905 14 366 *Ibid* 1906, 16 233
[3] Baar H *Z ges exp Med* 1926 50 601
[4] Brain W R *Lancet* 1954, i, 687
[5] Cave A J E, Griffith J D Whiteley M M *Ibid*, Jan. [illegible] 1955 p. 176

It is obvious that we desire to give the patient the best treatment for each phase we find him in, whether it be rest, support, manipulation, physiotherapy, or injections The patient, however, should be told that disc degeneration and its effects often progress along certain lines It is possible that treatment may influence its course, but sometimes bad effects occur, such as a transverse myelitis from a protrusion, in spite of all that is done, and in face of the best treatment possible Therefore, unless there is full understanding of the implications, the patient is liable to blame whatever treatment he is given for the inevitable worsening of his condition

London W 1 W E TUCKER

## PULMONARY HYPERTENSION

SIR,—In your editorial of Jan 15 you point out that cor pulmonale from multiple pulmonary emboli has been described, and quote an American reference [1] Valuable as is this Transatlantic report, your own columns did contain an earlier account of the same phenomenon [2]

London W 1 C P PETCH

## MOLLUSCUM PSEUDOCARCINOMATOSUM

SIR,—There was an interesting correspondence in your columns a year ago on this subject, which revealed some disagreement as to the frequency of the lesion Beare [3] and Stewart [4] gave estimates which suggested that as many as a third of the conditions ordinarily diagnosed in the past as squamous carcinomata of the skin were in fact mollusca, whereas Halnan [5] had seen only a single case He, and other radiotherapists with whom we have had the opportunity of discussing the matter, were unwilling to accept the suggestion,[6 7] which follows from the figures just quoted, that some revision of our ideas on treatment of squamous carcinoma of the skin may be necessary It seemed probable that this discrepancy might be susceptible of a very simple explanation that the sieving process—dare one say waiting-list treatment ? —that precedes entry to most radiotherapy departments might remove most of the mollusca, so that the condition might appear to radiotherapists such as Dr Halnan very much rarer than it does to those, like Dr Beare, who see the raw material

We have belatedly completed a survey of the material of our own radiotherapy department with the object of testing this idea The numbers involved are too few to justify a formal report but the results are of some interest

During the years 1942–51 our radiotherapists treated 83 cases under the diagnosis of squamous carcinoma of the skin We have re-examined the slides of all of these, and have been able to find only 3 mollusca (2 7%) Since 1952, when we began to recognise the lesion, 9 mollusca have been diagnosed, 3 from the radiotherapy department (against 30 squamous carcinomata), and 6 from surgical and dermatological departments (against 20 squamous carcinomata) This last figure, of 6 mollusca to 20 squamous carcinomata, agrees sufficiently well with Beare's estimate, and it is clear that, as we had suspected, mollusca are much rarer than this among cases coming to radiotherapy Statistics in this, as in so many matters are not transferable from one type of department to another

The error in diagnosis of squamous carcinoma tr by radiotherapy has one much more serious f There is a group of poorly differentiated skin tum usually regarded—by most histopathologists prob and certainly by us until about 1951—as poorly differ ated squamous carcinomata, but which we have lea to call instead rodent ulcers The group of 83 rep squamous carcinomata already mentioned incl besides the 3 mollusca, no less than 21 of these tod Among the 59 acceptable squamous carcinomata 9 recurred of the 21 re diagnosed tumours not one recurred, a difference much more easily reconciled their being rodents than with their being p differentiated carcinomata It is clear from these fi that there is scope for very great error in the as for any purposes of a series of cases of squa carcinomata of the skin

We would like to thank the members of our radioth department, and in particular Dr D N Edwards, for assistance in collecting data on these cases

Postgraduate Medical
School of London, W 12

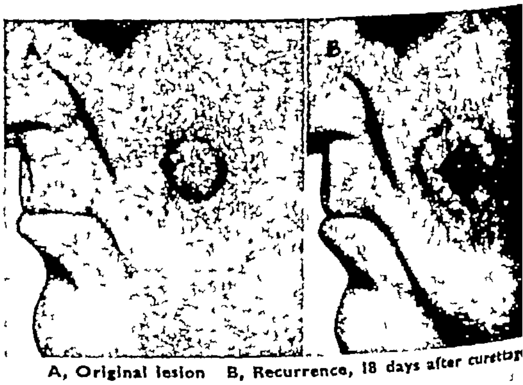
E LIBAN
BERNARD LENNOX

SIR,—In his paper on recurrent molluscum seba (Jan 22) Dr Beare has shown a tenacity to his ori diagnosis which has not been shared by others of cases where the lesion has recurred or rapidly incre in size after surgical interference This probably exp the absence of reported accounts of recurrent mollu sebaceum

The diagnosis of molluscum sebaceum rests on duration of the nodule, its appearance, and the equivocal histological characteristics In Dr Bea second case the lesion was of short duration and the clinical characteristics of molluscum sebaceum, it grew at an enormous rate after surgical interfer and was treated by radiotherapy

The following case, which resembles Dr Beare's sec case, illustrates the possible dangers of this diagnosis

A man, aged 45, attended this department on May 1954, with a nodule on the left cheek of three weeks' dur which was already almost 2 cm. in diameter In appear it was a typical molluscum sebaceum It was remov curettage on June 1 On June 18 the original area



A, Original lesion B, Recurrence, 18 days after curettag

surrounded by a thick, firm, rolled edge (see figure) A bio specimen was found to show "marked acanthosis pap matosis and hyperkeratosis with invasion of the corium large irregular columns of squamous cells The tumou producing epithelial pearls ' and there is a severe acut chronic inflammatory reaction to the invading cells. appearances indicate a grade 1 squamous epithelioma of check "

Treatment at the Sheffield Radiotherapy Centre was b on the same day with radioactive cobalt beam the (4800r in 21 days of daily treatment) After an m hyperkeratotic response the lesion healed by Nov 18, a remains healed this department I have seen almost as many of e cases as Dr Beare has collected and I am equally nced that molluscum sebaceum is an entity I am sure, however that in every case it is possible to nguish it from an epithelioma

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[1] Owen W R, Thomas W A Castleman, B Bland E F *New Engl J Med* 1953 249 919

[2] Petch C P *Lancet* 1951 i 1346

[3] Beare J M *Brit J Surg* 1953 61 167

[4] Stewart D T *Lancet* 1953 ii 1096

[5] Halnan K F *Ibid* p 1358 *Ibid* 1954, i 216

[6] *Ibid* 1953 ii 816

[7] [illegible] Lennox B *Schweiz Z Path* 1954 17 326

[8] Lennox B, Wells A L *Brit J Cancer* 1952 5 19

ay I suggest that only those lesions which ar ously becoming desiccated and shrinking should be ped off and that the fleshy rapidly growing lesions still best treated by radiotherapy despite the fact they may be molluscum sebaceum Let us retain he epithelioma the respect which it deserves

pert Hallam Department of
Dermatology
oyal Infirmary Sheffield

RONALD F CHURCH
Senior Registrar

## JUNIOR HOSPITAL STAFFING

R,—The draft report of the Strachan committee on nior ' hospital staffing together with Dr Forrester s nty report will by now have been seen by most ical members of the hospital services There is one ct of these reports which does not seem to have ived sufficient consideration—namely that a sub ultant grade which purports to offer a career in the ital services must offer to the newly qualified doctor ections comparable to those offered by general tice Otherwise the hospitals will be staffed largely failed general practitioners

onversation with contemporaries who are general titioners leads me to believe that a prospect of earning aximum of £2200 p a attained some 16 years after ification and without the income tax allowances h to general practitioners is one which compares vourably with the prospects enjoyed by the majority trants into general practice Further Sir, if the osed S.M O grade is adopted one wonders how long ill be before an economy minded Minister of Health s to use it as an inexpensive substitute for the ultant grade Adequate safeguards may be sought, ther would probably prove to be as worthless as the mmendations of the Spens Committee

A M READ
Assistant Chest Physician

smouth Chest Clinic.

## PIONEERS IN PSYCHIATRY

R,—The opening statement in your annotation of . 10 that ' three years after the fall of the Bastille ippe Pinel struck the chains from the lunatics in Paris Bicetre '' conforms with the traditional account ch has been copied from textbook to textbook down the most recently published History of Medicine it did not happen quite that way

Whatever dramatic action Pinel may have taken ediately after his appointment to Bicetre in 1793 r, not three years after the fall of the Bastille) clear from his own account that the abolition of chains the result of several years of patient work in the of difficulties and opposition Pinel says [1]

> The harmful effects of their use had given me much ern during the time I carried out the duties of Physician Bicetre, and it was not without extreme regret, that I nd myself unable to witness the termination of this tom custom [because of his transfer from Bicetre to the pêtrière] but on the other hand I felt quite confident, ing as I did in the skill of the Superintendent (M Pussin) se heart was as set as my own on putting an end to this ation of the true principles of treatment Success was ply achieved by him two years later on the 4th of rial, year 6 [May 1798] Forty unfortunate lunatics, had languished in irons for various lengths of time e set at liberty and allowed to move freely about the ng courts, with their movements merely controlled by the of the strait waistcoat.

It is perhaps not very clear whether the forty patients rred to were the final batch unchained in 1798 or total number liberated in five years Elsewhere [2] Pinel explains that the same result was achieved three years later (i e 1801) at the Salpêtrière again with the assistance of Pussin, who had been transferred at Pinel s special request

Cane Hill Hospital
Coulsdon Surrey

ALEXANDER WALK

## TUBERCULOSIS IN IMMIGRANTS

SIR,—Dr James in his letter of Jan 29 comments on the figures of tuberculin positivity in County Roscommon [1] It is admitted that the figure of 14 5% positive at 18 years of age is based on a statistically inadequate sample (69) but taken in conjunction with the other figures in our paper—namely 14 1% at 16 years (a sample of 249) 12 5% at 14 (404) 10 8% at 12 (852) and so on—it is evident that the whole picture for the county is one of a definitely tuberculin negative population group

We are in general agreement with the views expressed by Dr Hess and Dr Macdonald (Feb 12) about the susceptibility of the tuberculin negative immigrants and the greater risks which they run of becoming infected Like them we feel that progressive primary tuberculosis is not uncommon

We cannot accept Dr James s interpretation of the falling death rate in Roscommon The steep fall in recent years is in great part due to the considerable increase in the number of tuberculosis beds the more enlightened attitude of the people and improved methods of treatment Up to a few years ago the facilities for early diagnosis and treatment were totally inadequate The rate of 100 per 100 000 in 1943 was a war time peak. The rates for earlier years were much lower The Registrar General s return for 1950 [2] compares the tuberculosis death rates for the years 1925–27 and 1948–50 While the percentage fall for Ireland in the quarter-century was 38 7% that for co Roscommon at 10·1% was the lowest for the whole country It is probable that this slowing up in the rate of fall in Roscommon was due to the many migrants returning with tuberculosis.

We would like to see a similar change for the better in the morbidity rate This has not yet occurred though there is a shift to the older ages We agree with Dr James that this shift to the older ages indicates that tuberculosis is receding from the county but submit that this pattern will be found irrespective of whether a community has been heavily tuberculinised or only slightly as in the case of County Roscommon

In citing the lack of evidence of tuberculosis amongst the Irish in Commonwealth countries and the United States, Dr James is overlooking the fact that recent emigration from Ireland to these areas, compared with that to *Britain*, is rather small and is widely scattered over great continents. In addition this emigration is controlled and is largely sponsored in type the emigrant going to relatives and continuing family life It is not at all comparable with the figure of 30 000 native Irish who are reported to have gone to Birmingham to take one example since the end of the late war This immigrant group and the similar London group which were involved in the survey of Hess and Macdonald [3] are relatively easy to find No such recent Irish population group exists in the large cities of the New World

It is not an unusual experience in rural Ireland to find many members of a family infected by a returned emigrant Similarly we do not deny that the tuberculin positive Irish immigrant in Britain may be an epidemiological problem In fact it appears that the Irish in Britain live very much in one another s pockets so that a reactivation of disease in a tuberculin positive person may often be the source from which a large number of tuberculin negatives are infected

For this reason we suggest that in addition to B C G vaccination done if possible before emigration intensive mass radiography of immigrants should be pursued

Mullingar and
Roscommon

MICHAEL P FLYNN
J CYRIL JOYCE

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[1] Traité de l aliénation mentale 2nd ed. p 201
[2] *Ibid* preface p i

[1] Flynn M P Joyce J C *Tubercle* 1954 35 270
[2] Report of the Registrar-General 1950 Government Publications Office Dublin.
[3] Hess E V, Macdonald N *Lancet* 1954 ii 132

# Obituary

## CHARLES MARTIN

Kt., C M G , M.B , D Sc Lond , LL D , D C L , F R.C P , F R.S

Sir Charles Martin, director of the Lister Institute from 1903 to 1930, was a scientist of an unusual type He was born in London in 1866 and he studied at King's College and St Thomas's Hospital. He was an exhibitioner and London University scholar in physiology and the gold medallist of the year in that subject These early studies in physiology influenced his whole outlook on science and laid the foundation for his very various achievements in medical research. Throughout his career his general scientific grounding fitted him to undertake fruitful work in many different fields and gave his ingenious and original mind the necessary tools for each new task In addition he had much skill in inventing and constructing apparatus which served as tools for his hand

[J Russell

Soon after graduating in 1890 he went to Sydney as demonstrator in physiology in the university, and six years later he took the post of demonstrator in physiology in Melbourne, where he presently became professor As a teacher his methods were arresting and original, and his success in teaching physiology in the young medical schools of Sydney and Melbourne made his name and personality a legend and an inspiration to successive generations of students The lasting value of his influence was recently recognised when the Australian government founded fellowships bearing his name to enable young Australian medical graduates to obtain postgraduate experience overseas The gift of exposition and power to impart knowledge remained with him long after he had ceased to carry on any formal teaching

During these early years in Australia Martin found time to study the formation of antibodies to snake-venom He always regarded this as his most important piece of pure research, and it certainly laid the foundation of his scientific reputation It has particular interest as being concerned with the antibodies to a ferment, as enzyme complexes were still called in those days

While still in Australia, in 1901, he was elected a fellow of the Royal Society Two years later he returned to London on his appointment as director of the Lister Institute This post gave him full scope for his versatile powers During the next years his work included the study of typhoid and of plague He was chairman of the War Office Committee on Anti-typhoid Inoculation, and he had a large share in organising the work of the Advisory Committee for the Investigation of Plague in India which was appointed by the India Office, the Royal Society, and the Lister Institute He spent some time in India in the field in 1905

As a director of research he had the capacity to guide other workers without inhibiting them He had a fine insight into what was the essential point of a problem and great ingenuity in framing the appropriate experiments He also had a keen appreciation of the value of exact methods and applied the quantitative approach whenever it was possible This is well shown in his work on disinfection, which he carried out in collaboration with Dame Harriette Chick, and also in their work on the coagulation of proteins With his interest in the working of the animal machine, he recognised the import of Gowland Hopkins's early research on the growth factor, and work on the newly discovered accessory food factors (soon to be called vitamins) was already being carried out at the Lister in 1910 During the 1914-18 war this research grew into the nutritional department which, in a joint investigation wi Medical Research Council, was responsible for the able work on rickets done in Vienna by Dame Har Chick and her co-workers

In 1915 Martin had left the institute to jo Australian Army Medical Corps, and he served Gallipoli, Egypt, Palestine, and France. He di tinguished work in all these areas and became known for his resourcefulness in mitigating the mi of disease and for his efforts to investigate and co the spread of infection In military circles he wa held to be incorrigible in his originality in the of uniform the matter was finally left to his free choice, and he settled for the comfort of Australian private's uniform, though he held the of lieut -colonel.

On his return to civilian life he was unable to some formal recognition of his work In 1919 he appointed C.M.G for his war services In 1923 he re the Royal medal of the Society, and in 1927 he knighted The Universiti Edinburgh, Durham, and C bridge conferred on him hon degrees After his retir from the Lister Institute, he invited in 1931 to Au to become professor of chemistry and general phys and head of the division of nutrition in Adelaide Unive He held this post for three The last part of his life was in Cambridge, where he kept up interest in science and wa member of several M.R C. mittees and of the Wool Res Association

In the late war his gift hospitality found a wond application

The division of nutritio the Lister Institute, in he had always kept a fa interest, was obliged to ev itself from Chelsea, and accepted his invitation to m to his old house with its spa outbuildings on the edge of C bridge In former times the had been the Roebuck Inn and it was singularly priate for the purpose The changes needed to co conservatory into animal-house, and coach hous laboratory (familiarly known as the Medieval Lab), swiftly made under his supervision and to a large e with his own hands The work of the division permeated the house, even to his own room wher balances were set on a shelf securely fixed to the o wall Though some members of the division from to time found suitable accommodation in diff schools of the university, Roebuck House remained headquarters for more than five years In this inst in-miniature, the staff of the division continued to useful work in an undisturbed environment, and no could doubt that its old chief, despite his age and anxieties of the time, found happiness in the unexpe acquisition of this large family

Sir Charles Martin died on Feb 15 at his home Chesterton Lady Martin, formerly Edythe Cross, d last year They were married in 1891, and they le a daughter

### TRIBUTES

M R , to whom we are indebted for much of t memoir, writes

" As a person Charles Martin was free from affectatio any kind , he would not be bound by convention as to part of the work he tackled and he had a great feelin fellowship with the engineers and technical staff So left him undisturbed and he was without the faintest trac pompousness He had many warm friendships and he h the affection and trust of his staff He was quick to disco ir aptitudes and talents and was on the whole patient h their shortcomings and vagaries but was intolerant spurious and the pretentious. He always had great npathy with the needs and the outlook of the people with om he came in contact and was a staunch friend in disaster e gaiety and humorous outlook of his younger years was ldened by the 1914–18 war and he was only too prescient thinking that there would not be true peace again in his time."

H. C., who collaborated with Sir Charles in many vestigations, describes him as a 'great director t search.'

"He had a wide and deep knowledge of physiology and thology had followed closely the development of the new ences of bacteriology and immunity and had a useful quaintance with biochemistry and with many aspects of ysical and colloidal chemistry His varied gifts combined th the fruits of an accurate and retentive memory were ely shared with his colleagues. A mass of original work all high standard and much of great scientific importance ued from the institute while he was director Little of it ars his name though much was owed to his inspiration and ip He was the most generous of chiefs always anxious to rther the reputation of his juniors in preference to his own the young investigator needing advice his judgment was aluable in defining the type of question to which there was reasonable prospect of obtaining an answer and in limiting scope of the inquiry so that too many factors should t be involved. He saved the inexperienced from many itless efforts to investigate the universe as he would t it.

"Skilful with his hands he was never happier than when ooped in his workshop on the creation of some new gadget ended for domestic or scientific use Many researches in e institute owed rapid progress to the director's skill in ising new methods and producing some necessary and propriate piece of apparatus.

"His personality while often disconcertingly direct in anner and abrupt in speech was endowed with a whimsical arm and evoked warm devotion from all ranks. Like God was no respecter of persons and his subordinate staff red equally with his commissioned colleagues. Under s guidance the Lister Institute was a very pleasant and ofitable place in which to work.

L. J. H came to know Sir Charles as chairman, from 931 to 1946, of the committee of the Dunn Nutritional aboratory and to appreciate his astonishing width of terest and knowledge in the most varied fields of edical research."

"Equally at home in many specialised departments of athology physiology bacteriology or biochemistry he ad the gift of seeing right into the heart of a problem and knowing as he did how the present knowledge had been won, he equally sensed what gaps still remained to be filled n. He was interested in knowledge for its own sake and unlike some lesser men judged a research finding on its merits alone not by its authorship In consequence he was able to recognise talent and originality where others might miss it and, as a result, had the satisfaction of fostering young and sometimes precarious, research careers—leading in one instance at least to a Nobel laureateship His scientific integrity was marked by a robust sense of right and wrong and fair dealing combined with practical common sense He was prepared in no uncertain voice when occasion demanded to stand up against established authority when he knew that authority to be in the wrong and his courageous determination more than once won the day

"Although in his own tastes simple to a degree he could prove himself a man of the world in dealing with officialdom He himself had the gift of handling men and of dealing effectively with committees and organisations: indeed one of his maxims was that people who failed to rub shoulders with their contemporaries had not succeeded in learning one of the elementary techniques of their trade Another of his maxims was that it is useless to appeal to reason where a person's emotions have become involved

"To the end he retained both his charm and penetrating intellectual faculty and it was an experience to hear him at the end of the ninth decade of his life giving his stimulating comments on some future scientific developments which he foreshadowed after reading a paper that had just appeared in a current issue of a scientific journal

## OSWALD THEODORE AVERY

### M.D Columbia For Mem. R.S.

Dr Oswald T Avery, the distinguished American bacteriologist, died at Nashville Tennessee on Feb 20 at the age of 77 His brilliant researches into the structure and serology of pneumococci will be remembered as the starting point of some of the most important advances in modern immunology

Avery graduated at Columbia University, New York, in 1904 and he soon displayed that skill in applying chemical methods to bacteriology which was to produce such valuable results In 1918 with his colleague, A R Dochez he began a long study of the antigenic structure of the pneumococcus by serological methods. In 1923 he interested Heidelberger and a number of other chemists in the chemical differences between pneumococci of different antigenic structure and a new field in serology was opened up In their first paper his team described a complex polysaccharide obtained from smooth pneumococci, and this substance was shown to be responsible for the reactions between pneumococci and antiserum It was not, however, antigenic for its injection into animals did not produce antibodies. They later found that the polysaccharide was not specific to the pneumococcus but was identical with similar substances in yeast or gum arabic which also reacted in the test tube with antipneumococcal serum Though the polysaccharide was not antigenic, it could be coupled with other substances—for instance, horse-serum globulin—and then became antigenic and even capable of protecting animals from a fatal dose of pneumococci

These advances were the result of an organised attack on respiratory diseases, of which Avery was the leader, and the striking progress achieved was largely due to his stimulus He showed the way to later developments which are now making it possible to interpret immune reactions in terms of exact chemistry

For many years Avery was a member of the Rockefeller Institute in New York In 1941 he was elected a foreign member of the Royal Society and he was awarded the society's Copley medal in 1945

## CLAUDE RUNDLE

### O B E., M.D *Lond.*, D.P H

As superintendent of the isolation hospitals at Fazakerley Dr Rundle was associated with the Liverpool city hospital service for close on thirty years.

He was born in 1873 at Plymouth and educated at the Grammar School of that city In 1895 he qualified from St. Mary's Hospital and he graduated M D Lond three years later Almost at once he joined the public health service, and his first appointments were with the Metropolitan Asylums Board as medical officer at Gore Farm Convalescent Hospital Dartford and as senior assistant medical officer at the Grove Fever Hospital Tooting In 1901 he took the D P H About this time he became medical superintendent of the Orchard Smallpox Hospital Dartford, and in the great smallpox epidemic of 1901 he served on the hospital ships stationed in the Thames estuary for the emergency

These early experiences naturally led him to choose infectious diseases as his life's work. In 1901 he took his M D and two years later he was appointed the first medical superintendent of the isolation hospitals at Fazakerley He organised the main isolation hospital of 350 beds which was opened in the year he arrived Later the annexe hospital which had been built some years before was added to make a complete unit which was to become known throughout the country

Dr Rundle held a commission in the Territorial Army from 1908 and in the first world war with the rank of lieut.-colonel he commanded the Berrington War Hospital He was also responsible for about 100 auxiliary units scattered over Western England and Central Wales. For a time he commanded No. 53 General

Hospital in France, and for his services he was appointed O B E in 1919 J M, who first met him at Berrington Hospital, writes

"On his medical staff he had two Irishmen, north and south respectively, an elderly fundamentalist, a thoroughly businesslike medical officer, and me He kept us all in good humour, including the commandants, with amazing skill He was a very dignified figure with a long face and a moustache, a slight droop on one side of his mouth, perhaps due to an old facial paralysis, gave him a somewhat supercilious manner in appearance and speech This he used to full advantage to confound the evil doers—that is, slackers and pretenders In hours of work he was firm and efficient, never wasting a word, but in the evenings when we sat at mess he used to delight those who were not his victims by playing us against one another, especially the realist against the fundamentalist His method was to make some outrageous statement that stirred up some member of the mess, and he then conducted the quarrel like an orchestra reaching a conclusion that brought inextinguishable laughter all round The commandants one and all adored him I am sure this was not because he was at that time a bachelor but on account of his infinite charm, patience, and courtesy He used to bring us home tit bits in his pocket from his more wealthy clients and invent droll fairy stories about them

'Rundle knew every patient personally and he could sometimes be quite disconcerting by showing greater clinical insight about a sick man than the medical officer who was in charge, but he never interfered—he only asked"

Soon after his return to civilian practice a large sanatorium of 265 beds was opened in 1920 on the Fazakerley estate and as superintendent of the whole group of hospitals he had charge of some 900 beds For many years he was also lecturer in infectious diseases at Liverpool University He revised the third edition of *Ker's Manual of Fevers* (1927) and the third edition of *Ker's Infectious Diseases* (1929) His published work included papers on bed-isolation methods, a technique in which he was a pioneer He was a deputy lieutenant of the county of Lancaster

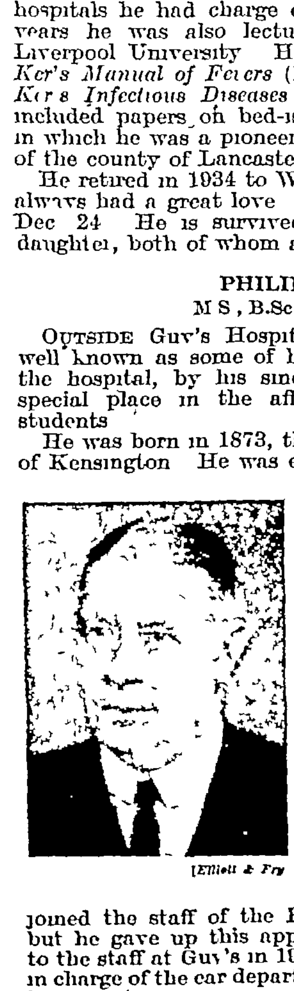
He retired in 1934 to West Looe, a place for which he always had a great love He died at his home there on Dec 24 He is survived by his widow and married daughter, both of whom are doctors

## PHILIP TURNER

M S, B.Sc Lond, F R C S

OUTSIDE Guy's Hospital, Philip Turner was not so well known as some of his contemporaries; but within the hospital, by his sincerity and loyalty, he won a special place in the affection of his colleagues and students

He was born in 1873, the son of Arthur James Turner, of Kensington He was educated at King's College and University College, graduating B SC with honours in zoology He continued his medical studies at Guy's Hospital, where he held an entrance scholarship He won many of the prizes open to students, and finally gained the treasurer's gold medal in clinical surgery While holding house-appointments at Guy's and a clinical assistantship at Great Ormond Street, he prepared himself for the higher surgical qualifications, and in 1901 he took the M.S and F R C S In 1902 he was appointed registrar at Guy's and the following year demonstrator in anatomy In 1904 he joined the staff of the Belgrave Hospital for Children, but he gave up this appointment when he was elected to the staff at Guy's in 1908 There for two years he was in charge of the ear department. Later he became lecturer in operative surgery As an assistant surgeon for seventeen years he had only a small number of beds and somewhat overshadowed by the dominant personality of his senior, Sir Alfred Fripp He held appointment of full surgeon for eight years, and attained the honourable position of senior surgeon a fortnight before he retired He contributed art to many well-known surgical textbooks, and his oth publications included *Operations of Surgery*, *Po Osteology*, and *Inguinal Hernia*



[Elliott & Fry

During the late war he returned to work in the Guy sector as a senior surgeon in the Emergency Med Service at Joyce Green Hospital After the war retained his interest in the hospital, and, as his recept as chairman of the Guy's biennial dinner a few mo ago showed, his place in the memory of Guy's men

N L E writes

"Philip Turner had a dry and retiring personality, he was seldom seen at extramural activities But within hospital there could be no more devoted servant Ev patient under his care became his personal concern, and detail too small to be noticed. He was neat and metic in all his work, and those who were on his firm are m grateful for his lessons in technique He had a prodig memory, and nothing gave him more pleasure than to reco with exactness of detail, incidents and case histories fr his long experience In the 1954 Christmas number of *Guy's Hospital Gazette* he recounted his experiences as a lo some fifty years ago, as if they had just happened

"Turner was never known to say ill of anyone He an extremely lovable man, and like a father to all who wor under him"

Few people will remember Philip Turner as a you man (writes W H O)

"When I came to Guy's as a student he must have be in his thirties, but he seemed to be weighed down already w the seriousness of life and the importance of surgery, with t gravity of the decisions he had to make and the example must set to the young I do not believe he ever poss a motor car He always came by tube or bus, and he was nev late He dressed in morning coat He spoke with the utmo earnestness, and even when he allowed himself to make joke, he announced it seriously, explained it carefull and after marking its climax by a restrained and form chuckle, he hastened to return to his previous mood solemnity

"There is no place comparable to a medical school fo the correct assessment of values, no psycho analysis mor penetrating than that of the unformulated judgment o several generations of students Philip Turner's capac for work, his unfailing sense of duty, his knowledge of anato and of surgical history, his gift of clear exposition ear him respect, and his obvious sincerity and his loyalty to hospital and his students earned him affection And in th affection he blossomed His approach became less form his jokes more spontaneous and more frequent, and in last ten years he developed social gifts and a capacity fo enjoyment that made him one of the most popular men o his time"

His wife, formerly Miss Helen Lambert, predeceased him in 1932 He died on Feb 16 at the age of 81

## Colonel A E HAMERTON

R E R writes "Hamerton was a very remarkable person He was one of the last generation who still regarded India and Africa not just as places to work in but as areas for inspiration and adventure He might well have stepped out of the pages of Rider Haggard. His life was packed with adventure and I remember him saying 'I don't care what they take from me, they cannot take my memories' His quality is, I think, best revealed in his confession that even when working for the Sleeping Sickness Commission he could never bring himself to shoot a giraffe it was far too beautiful"

In our obituary of Colonel Hamerton (Feb 12) the inadvertent omission of the words "an outbreak of" suggested that he was the first to describe acariasis in monkeys. Mites were identified in monkey's lung as early as 1901 and a description of the infestation was published by Helwig in 1925

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A memorial service for Sir Edward Mellanby will be held at St Martin in the Fields at 11 30 A M on Thursday, March 17

# Notes and News

## ACTIVITIES OF F A O

n the early days of the United Nations optimists with gination hoped that the Food and Agricultural Organisa t, under the directorship of Boyd Orr might find grand itions for the urgent problem of providing sufficient food for the ever increasing population of the world The latest F A O report[1] shows that such hopes have become pi ams. Perhaps there are no grand solutions Yet F A O either idle nor disillusioned Instead it has settled down l assumed the function of a large scale scholastic agency ling in technical education and education is a slow ess, which cannot immediately give startling results

n 1954 F.A O was responsible for the selection organisa n, and partial payment of over 200 experts, who visited ious foreign countries to help with technical advice Since l nearly 800 experts have taken part in such missions Early in 1954 about 140 fellowships were awarded to ble persons to receive special technological training which not available in their own country The experts advised uch diverse fields as improvement of hide and skin process in Libya, irrigation in East Pakistan fisheries develop at in Chile and ground water development in Syria lowships were awarded to an Israeli for the study of milk giene in Denmark and Sweden, to a Nepali to study dairying l animal husbandry in New Zealand to a Yugoslav to dy home economics in Holland and France to an Egyptian study rice production in Japan and to two Thais to study icultural economics in the U S.A. These are only a few the large body of carefully selected fellows and experts o are continually travelling about the world receiving and tributing technical knowledge They must be making a d contribution to material prosperity in many underveloped countries. Perhaps equally important they are rt of an international system for the exchange of ideas d good will, and so they contribute to international undernding. It is unfortunate that the budget for this work l from $6 049 000 in 1953 to $5 536 000 in 1954. The work pends on the assistance of countries contributions to the chnical Assistance Fund—and first and foremost that of United States. If this work is to be carried on it must ve the good will and support of responsible citizens in ery part of the world.

## BLOOD-COAGULATION AND THROMBOSIS

The latest issue of the *British Medical Bulletin*[2] gives a luable and candid survey of present British views on the ndamental problems of blood-clotting blood vessel thromsis, and the use of anticoagulants. British workers have ade notable contributions to this subject during the past ten years or so and anyone who wishes to set out on further ork from an up to-date base cannot do better than read the ticles in this issue.

## LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE

The report of the work of the school in 1953–54[3] emphasises am the international scope of its activities. A large number overseas visits were paid by senior members of the staff for the purposes either of consulting with foreign colleagues interested in a particular aspect of research or of attending international conferences Dr Andrew Topping the dean, and Prof G Macdonald director of the Ross Institute of Tropical Hygiene visited the site of the proposed dam across the Volta River in the Gold Coast; their report on the health problems involved included a detailed specification of the preventive curative and industrial medical services for two major labour forces and for the new town to be built in the vicinity of the dam. The school's various training-courses have once more had a full quota of students. The number of candidates for the D.T.M. & H. courses has remained much the same as last year but there have been more entrants for the D.P.H. course with tropical medicine as the elective subject Greater emphasis has this year been laid on industrial medicine in the course on public health and the scope of the elective course in industrial health has been widened The report includes a summary of the research done during the year in the various departments

## CONVALESCENT HOMES FOR LONDON

King Edward's Hospital Fund[1] have published the 1955 edition of their *Directory of Convalescent Homes* serving Greater London The first part includes homes within the four Metropolitan hospital regions the second part lists homes outside the regions which are prepared to admit patients from London Useful classified indexes will enable the busy doctor to choose in a moment for instance a home for a middle aged gentlewoman with asthma who wishes to go to Broadstairs and have breakfast in bed

## EXHIBITION OF HEARING-AIDS

The modern electrical hearing aid consists of a microphone an amplifier and a receiver small dry batteries supply the current Much ingenuity has gone into reducing the size and weight of the components and into prolonging the life of the batteries The Medresco aid[2] which is issued on free loan under the National Health Service has undergone several such modifications in the last few years and some of the different patterns now available were displayed at a small exhibition held last week in London by the Ministry of Health

The earlier models though still widely used are gradually being replaced by lighter and more efficient instruments. Last year for example the supplies division of the Ministry issued no fewer than 200 000 new hearing aids, 4 000 000 batteries and 60 000 ear moulds and over 1 000 000 other components Latest figures show that nearly 400 000 persons have been provided with medresco aids. Nevertheless waiting lists remain large chiefly because of the difficulty in issuing the instruments quickly enough from the 60-odd centres throughout the country

The newest model on view—the medresco monopack—has been specially designed for children Little larger than a packet of ten cigarettes it weighs only a few ounces, and runs off a battery less than $1^1/_2$ in. long Field trials will begin shortly and if they are successful the instrument will go into mass production. Also on show were a number of different patterns of ear trumpet Not surprisingly these retain a degree of popularity among older patients, and more than 1000 were issued by the Ministry last year

### University of Sheffield

At the jubilee congregation to be held in the city hall on Wednesday June 29 1955 the honorary graduates will include Lord Adrian O.M., P.R.S who will receive the honorary degree of D.Sc

Dr O G Dodge has been appointed lecturer in pathology The title of reader has been conferred on Dr Gilbert Forbes, at present senior lecturer in charge of the Department of Forensic Medicine

### Royal College of Surgeons in Ireland

Over two hundred fellows and guests attended the annual charter day dinner of the college on Feb 12 The toast of The Guests, who included the Surgical Travellers Club was proposed by Mr A. B Clery the vice president and Prof Eric Ashby vice-chancellor of the Queen's University Belfast and Sir Stanford Cade replied The toast of The College was proposed by Sir Heneage Ogilvie and Mr Ian Fraser the president replied

On Feb 18 the fellowship was conferred on the following

J S R. M. Lavelle F N O'Connell

### Society for General Microbiology

The general meeting of this society will be held at the Royal Institution, Albemarle Street London W 1, on April 18–20 On Monday the 18th at 6 P.M., Prof C B Van Niel of the Hopkins Marine Biological Station California, is to give the Marjory Stephenson lecture on Natural Selection in the Microbial World Visitors will be welcome to this lecture On Tuesday and Wednesday the 19th and 20th there will be a symposium on mechanisms of microbial pathogenicity Further particulars may be had from the society c o the Institute of Biology Tavistock House South, London W C 1

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[1] Activities of F A O under the Expanded Technical Assistance Program 1953–54 F.A.O Rome December 1954

[2] *Brit. med. Bull.* 1955 11 no 1 London: The British Council. Pp 81 15s

[3] Report on the Work of the School for the Year 1953–54 London School of Hygiene and Tropical Medicine (University of London) incorporating the Ross Institute Keppel Street Gower Street London W C 1

[1] Copies may be had from the office of the Fund, 10 Old Jewry E C 2 7s 6d (post free)

[2] Gray I G Cartwright A *Lancet* 1951 1 1170

### Research Board for the Correlation of Medical Science and Physical Education

The board announce that the William Hyde Award of £300 has been given this year to Dr Roger Bannister for his studies of physiological reactions to stress

### World Health Organisation

World Health Day, which will be celebrated in most countries on April 7, will have for its theme Clean Water Means Better Health

### West End Hospital for Neurology and Neurosurgery

A course of clinical demonstrations in neurology is to be held at this hospital, 91, Dean Street, London W 1, on Tuesdays at 5 30 P M from March 1 to May 10 Admission is free and the demonstrations are open to doctors and students

### Committee on Trial Case Lenses

The Minister of Health has appointed a committee to review "standards for trial case lenses and the method of measuring lens powers and to make recommendations" The medical members are Sir Stewart Duke Elder (chairman), Mr J E Ayoub, and Mr F W Law

### Basingstoke Plastic Centre Medical Society

On Thursday, March 10, at 7 30 P M, at Rooksdown House (Park Prewett Hospital), Basingstoke, Mr N L Rowe will take the chair at a symposium on *Fractures of the Middle Third of the Facial Skeleton* The speakers will include Mr R S Lawrie, Mr M A Falconer, Dr R P W Shackleton, Mr H C Killey, Mr Gordon Midgley, and Mr B W Rycroft

### French Exchange Scholarships

Under the terms of a reciprocal arrangement with the Centre National de la Recherche Scientifique, the Medical Research Council invite applications from British workers in medical science, excluding clinical medicine, for two scholarships tenable at research institutions in France during 1955-56

The scheme is intended for young graduates in medicine or science who have already had some experience in a branch of medical science Candidates must be of British nationality and have at least a working knowledge of French The scholarships will normally carry a maintenance allowance of 50 000-70 000 francs a month and married men will receive a supplementary allowance Forms of application may be had from the Secretary of the council, 38, Old Queen Street London S W 1 with whom applications must be lodged by March 31

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## Appointments

DREW, C E, M V O, M B Lond F R C S part time consultant thoracic surgeon, St George's Hospital London

SCOTT, A. E R M R C S asst M O, and deputy M O H, Slough

**Leeds Regional Hospital Board**

CUMMING, A R. R M D Aberd, M R C P E whole time consultant geriatrician Hull and East Riding

SUFFERN, W S M D Leeds, M R C P part-time consultant in general medicine and geriatrics, Bingley, Keighley, Skipton, and Settle area

TODD JOHN M B, D P M whole time consultant psychiatrist Menston Hospital, near Leeds

WATERS, G W M B Manc D P M whole time asst psychiatrist and deputy medical superintendent (S H M O) Meanwood Park Hospital, Leeds

WHITE J M M D Glasg D P M consultant psychiatrist and deputy physician superintendent Stanley Royd Hospital, Wakefield

**Sheffield Regional Hospital Board**

BREST SIMON M B Wales D P M whole time senior asst psychiatrist Carlton Hayes Hospital, Narborough near Leicester

FORREST B G M B St And D A consultant anæsthetist Rotherham and Mexborough H M C

HOLDWAY VERA M R C S, D P M whole time senior asst psychiatrist, Carlton Hayes Hospital

**North East Metropolitan Regional Hospital Board**

CLARK, A S M B Lond D P M part time consultant psychiatrist Edmonton child guidance clinic

JENKINS W J, M D Wales whole time consultant pathologist and medical director Brentwood Blood Transfusion Centre

JOHNSON J H P M B Calcutta, M R C I whole time consultant chest physician Tottenham chest clinic

WHITEHEAD J P S M R C S whole time consultant pathologist, Tilbury and South East Essex group

**Appointed Factory Doctors**

ARNEY K B M B Brist Kingwood, Gloucester
CARMICHAEL G A M B Glasg D OBST Kirkmichael Banff
JOHNS B A E M B Birm M R C P Sheffield West, Yorks
JOYCE THOMAS M B Edin M R C P I Troon Ayr
LYNCH A D M B Glasg Kilwinning, Ayr
PAUL, J G S M B Edin Inveravon Banff
RITCH, D R. S M B St. And Alloa Clackmannan
TILSLEY D A M R C S Sheffield 6 Yorks

## Diary of the Week

FEB 27 TO MARCH 5

### Monday, 28th

MEDICAL SOCIETY OF LONDON, 11, Chandos Street W 1
8 30 P M *Mr Denis Browne Mr Nils Eckhoff* Common C genital Deformities
MANCHESTER MEDICAL SOCIETY
9 P M (Medical School) *General Practice* Dr F R. Fo Migraine and Epilepsy

### Tuesday, 1st

BRITISH POSTGRADUATE MEDICAL FEDERATION
5 30 P M (London School of Hygiene and Tropical Me Keppel Street, W C 1) Dr C H Andrewes F.R.S. Look in Virus Research.
ROYAL SOCIETY OF MEDICINE 1, Wimpole Street W 1
5 P M *Pathology & Epidemiology and Preventive Medicine.* Theodore Crawford Dr J E French Prof H W Fu Dr J N Morris Coronary Artery Disease
8 30 P M *Orthopædics* Mr R. Weeden Butler Vert Osteochondritis (Presidential address)
ST MARY'S HOSPITAL MEDICAL SCHOOL, Paddington W
5 P M Mr John Beattie Abnormalities of Bladder Functi
INSTITUTE OF DERMATOLOGY St John's Hospital Lisle Street,
5 30 P M Dr C Hodges Superficial X ray Therapy

### Wednesday, 2nd

ROYAL SOCIETY OF MEDICINE
5 15 P.M *History of Medicine* Dr Ffrangcon Roberts E of Epidemics on Population and Social Life
8 P M *Surgery* Mr C Naunton Morgan, Prof J C. Go Mr Ralph Marnham Minor Ailments of the Anal C
INSTITUTE OF DERMATOLOGY
5 30 P M Dr R W Riddell *Trichophyton rubrum* Infecti
INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330 Gray's Inn W C 1
6 P M Dr H Engström (Stockholm) Anatomy of the Co by the Electron Microscope
MIDLAND MEDICAL SOCIETY Birmingham Medical Institute, Great Charles Street Birmingham 3
8 15 P M. Dr J F Brailsford Lesions of the Interver Discs
LIVERPOOL MEDICAL INSTITUTION
4 30 P.M (Joint meeting with the Manchester Medical S at the University of Manchester) Prof A. W Do Virus of Chickenpox and Herpes Zoster Dr C A C Methods of Investigating Inherited Factors in Disea
MEDICO-CHIRURGICAL SOCIETY OF EDINBURGH
8 30 P M. (Royal College of Surgeons 18, Nicolson St Dr A G MacGregor Dr C F Rolland Hypopituit

### Thursday, 3rd

ROYAL COLLEGE OF SURGEONS OF ENGLAND Lincoln's Inn W C 2
5 30 P M Mr A J Gardham Evolution of Major Surg the Mouth and Pharynx from the time of Trotter t Present Day
ROYAL SOCIETY OF MEDICINE
8 30 P.M. *Otology* Mr Terence Cawthorne Otosclerosis ( lecture)
ROYAL ARMY MEDICAL COLLEGE Millbank S W 1
5 P.M Dr J F Loutit Acute Radiation Syndrome
UNIVERSITY OF ST ANDREWS, Medical School, Small's W Dundee
5 P M Dr F G Spear Use and Misuse of Radiation

### Friday, 4th

POSTGRADUATE MEDICAL SCHOOL OF LONDON, Ducane Road, W
2 P.M Mr R W Raven Malignant Melanoma.
ROYAL SOCIETY OF MEDICINE
10 30 A.M *Otology* Dr Sölve Welin (Malmö), Mr W I Da Mr I Simpson Hall Radiology of the Temporal Bone
2 30 P M. *Laryngology* Mr H P Lawson Mr Neville You Bilateral Abductor Palsy Mrs Florence Cavanagh Vo Palsies in Infancy
5 30 P M. *Anæsthetics* Dr H C Churchill Davidson Abnor Responses to Muscle Relaxants
INSTITUTE OF DERMATOLOGY
5 30 P M Dr P D Samman Lichen Planus
METROPOLITAN EAR NOSE, AND THROAT HOSPITAL, at St Mar Abbots Hospital, Marloes Road W 8
5 30 P.M. Mr Terence Cawthorne Surgery of the Ear (Jame Yearsley lecture)
ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASGOW, 242 St Vincent Street
5 P M Mr Matthew White Thoracic Surgery in Children

### Saturday, 5th

INSTITUTE OF LARYNGOLOGY AND OTOLOGY
NOON Dr Engström Anatomy of the Vestibule by the Electro Microscope

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CORRIGENDUM *Argentaffinoma as Endocrine Tumour*—In the letter by Dr I H. Page and others (Jan. 22, p 198) the name of Dr Albert Sjoerdsma was incorrectly spelt. Th last three signatories wrote from the National Heart Institute Bethesda 14, Maryland

# PATHOLOGY OF REHABILITATION*

P B S FOWLER
D.M Oxfd M.R C P
ASSISTANT PHYSICIAN CHARING CROSS HOSPITAL

effect of physical and mental disease on rehabilita and the relative importance of different factors mpede resettlement, have been studied in 1945 d persons. These were a representative sample of tal register of disabled persons for the south east gland—the register set up in 1944 under the Dis- Persons (Employment) Act The material thus from a unique source very different from the al practice upon which most work on disabilities en done

he 1945 people, 40% were not under any medical or their disability 33% were attending their own only and 27% were under hospital care or ling special clinics A cross section of disabled s taken from hospital or general practice in this y would undoubtedly show a higher proportion ere disease than is found among the disabled s registered under the Act but there is no close ation between the severity of a disease and the lties in attaining resettlement. The Disabled ns Register gives a balanced picture, not of dis es in this country but of the problems of resettle of disabled persons in industry They are admitted register either because they need the help offered e Act to overcome resettlement problems or—if are already employed—because they need security k in open competition with the healthy

selection of the sample and the method of survey been described elsewhere (Fowler 1953)

### Resettlement

settlement is defined as the more or less perma placing of a person in an occupation after disability

developments are possible after disablement ilure to become resettled (i e , unemployment or lity to remain in steady employment) (2) unsatis y resettlement and (3) satisfactory resettlement her resettlement is satisfactory or unsatisfactory e assessed by the criteria of earnings, social prestige ork, and suitability of the occupation on medical ds. The first two can be evaluated by comparing with the person s earning and prestige before he disabled (Fowler 1953) (In many cases, however assessment was not possible for instance when atient had been disabled as a child no comparison ork before and after disablement could be made )

the 1945 persons seen in this survey 716 (36%) were ployed 1229 were employed but in 216 resettlement not be assessed by the method adopted Of the remaining employed cases resettlement was unsatisfactory in 152 and satisfactory in 861 cases. Resettlement in 113 of 15 cases was unsatisfactory because of social status of and income In 21 cases the work was unsuitable on al grounds, and in 18 cases resettlement was unsatis y on both medical and socio-economic grounds.

he low incidence of unsatisfactory resettlement on ical grounds of those in work suggests that disabled ttlement officers (D R O ) do not recommend disabled ons to go into medically unsuitable work and that disabled person seeks medical advice before taking loyment There was, however also a strong impres that of the 716 unemployed persons seen many had ed employment for medical reasons when what they ly needed was reassurance that a wide range of work within their physical capabilities and would do them no harm. It is as important for the disabled person to be told what he can do as what he cannot do : 20% of those seen who were on the disabled person's register had disabilities " which did not handicap them in their work and they should never have been admitted to the register Of these 408 people 16 were unemployed

Of the 861 disabled persons who were satisfactorily resettled 589 had jobs in which the income and prestige from the work was the same as before disability and the job was medically suitable In 124 cases the work was superior and in 148 in some respect inferior to that before disablement. Of those who had had special training 30% had improved their position since disablement as compared with 8% of those without special training

### The Quota

A disabled person for purposes of registration is defined in the following terms

> A person who on account of injury disease or congenital deformity is substantially handicapped in obtaining or keeping employment, or in undertaking work on his own account of a kind which apart from that injury disease or deformity would be suited to his age experience and qualifications

The definition, in fact is made in terms of *employability* and the character of the register depends on this interpretation

It could be argued that a company director with an amputated left arm should not be considered " disabled " as defined by the Act while a docker with the comparatively trivial deformity of flat feet might be severely handicapped in doing his normal work Usually however the specific disease or injury alone and not the disability, has been made the basis for registration In assessing a disabled person s handicap the disability should be considered, not in its own right but in relation to the work to which he is accustomed and suited Using this criterion I have graded the people in this sample as follows

| | *Grade* | *Employed* % | *Unemployed* |
|---|---|---|---|
| I | Disability has no effect on the type of work to which the person is suited and normally carries out | 20 | 1 |
| II. | Handicapped by their disability in keeping or finding suitable employment | 37 | 16 |
| III. | So severely handicapped that they are fit only for sheltered work | 5 | 11 |
| IV | At time of interview unemployable | | 9 |

It will be seen that 20% of the sample is placed in grade I which is outside the definition of disabled as laid down by the Act These include some unemployed who are receiving the specialised help which should be reserved for disabled persons, as well as many employed who are filling the quota for employers and preventing the truly disabled from getting work Employers, many of whom have voluntarily helped disabled persons in the past naturally believe they are carrying their responsibility if their quota is filled

With the quota at 3% saturation point has nearly been reached, yet the total register continues to grow The proportion of employed to unemployed is far higher in grade I than in grade II, and unless registration is made with more care the tendency will be for the fixed number of disabled job vacancies to be completely filled by non-disabled persons The substantially handicapped unable to obtain any benefit from the quota system will remain unemployed Raising the quota to 4 5 or 20% would offer no solution since for every disabled person in grade I on the register 20 or more would have equal claims to be admitted The quota system can be effective only if the definition of disabled as laid down in the Act is stringently applied

To find the cause of wrongful registration a study of the initiation of registration has been made It was

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s work was done under the aegis of the Medical Research Council and was described in a thesis for the degree of D.M.

TABLE I—THE STIMULUS TO REGISTRATION OF 1945 DISABLED PERSONS

| Employability grades | Doctor | Employer | Employment exchange | Self | Ex-Service pensioner | Total |
|---|---|---|---|---|---|---|
| I | 41 | 132 | 81 | 92 | 50 | 396 |
| II | 169 | 188 | 319 | 193 | 113 | 982 |
| III | 78 | 26 | 143 | 43 | 52 | 342 |
| IV | 27 | 5 | 52 | 15 | 16 | 115 |
| Total | 315 | 351 | 595 | 343 | 231 | 1835* |

* In addition the stimulus to registration was a trade union in 8 cases other agencies in 25 cases and was not recorded in the remaining 77 cases (total 1945 cases)

most often unjustifiable when initiated by the employer (table I)

Of the 315 persons whose registration was initiated by doctors 13% were not disabled  Of the 595 persons registered on the advice of the employment exchanges, 13 4% were not disabled  The corresponding percentage for those registered on the advice of their employers was 37 6  Employers took advantage of the lay interpretation of the word "disabled," but in no case was there evidence that an employee had been *forced* to register as disabled  In 1946 the Ministry of Labour sent a circular to all employers drawing their attention to the need to register all disabled persons, and 1946 became the peak year for registration—the year in which most of the people with trivial disabilities were allowed to register

At the other extreme, of those with a disability so severe that they were unemployable the highest proportion were registered on the advice of doctors (table II) D R O s complain that they are forced to spend much time in trying to place disabled persons who are obviously unemployable, very often with a psychological disability and in need of psychiatric treatment

### Rehabilitation

Rehabilitation is here defined as "the active process that leads to the restoration of the handicapped to the fullest physical, mental, social, vocational and economic usefulness to which they are capable"  Rehabilitation is not used as synonymous with rehabilitation therapy  Complete restoration of the handicapped person can and often does occur without outside assistance, but rehabilitation has nevertheless taken place  Rehabilitation therapy is defined as "all measures taken to further this active process of rehabilitation"

Social disease is discord between the individual and his social environment, and the treatment of social disease, like that of organic disease, should be based on an understanding of its pathology and the factors that produce discord

The failure to exist in a healthy relationship with the social environment is by no means always secondary to organic or mental disease  Certainly most persons who need resettlement are not physically handicapped  Even in a survey of persons chosen because they were disabled, the disability was often incidental to other factors preventing resettlement

### The Sexes

Of the 1945 disabled persons studied, 10% were women  Women present fewer problems than men, not only because there are fewer of them in industry, but for three other reasons  First, as the demand for women at present exceeds the supply, women are able to pick and choose their work  Since much of it is monotonous, they have little hesitation in giving it up, confident that in a short time they can quickly fall into other suitable employment  Secondly light work suitable for the physically handicapped is traditionally reserved for women  (Only 1 woman in this survey was in work that was medically unsuitable )  Thirdly, part-time work is available for women, because healthy women with household duties are unable to enter industry ex this basis  This important therapeutic tool, br the gap between convalescence and return to full is difficult to arrange for men

Of the employed men, 2% were doing part time wo compared with 12% of the women  Despite the circums which make the resettlement of disabled women easier that of men, 45% of the women, as compared to 36% of men, were unemployed  There is of course less married women to find employment than for men. employed women only 5%, as compared with 16% of were in unsatisfactory work

### Age-incidence

The extra handicap of age to the disabled per shown by the employment figures for the [illegible] groups

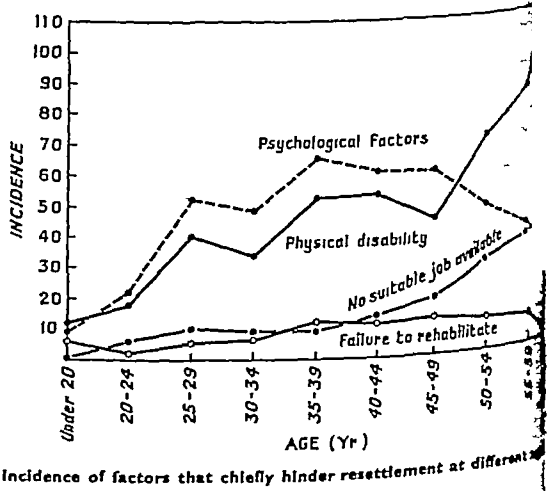
For disabled persons under 40, less than a quarter unemployed, for the groups aged 40 and over, more half were unemployed  With increasing age, loss of a bility narrows the field of suitable work, even in the of full employment, many people over 40 not handicapp disability are finding it hard to get work  Comparing figures for the country for men unemployed for over a y Dec 5, 1949, there were 6000 under the age of 41, as co with 13,000 between the ages of 41 and 56 and 15,00 56 and over (*Ministry of Labour Gazette* 1950)

Of the total number of cases (911) in the survey o age of 45, 29% were fit for sheltered work only and 4 selected open competitive work, of the total number of (1034) under the age of 45, 11% were fit for sheltered only and 59% for selected open competitive work

Age plays the causal rôle in the large group of deg tive diseases and is an aggravating factor in disabilities  A wide choice of occupation, the es need in resettlement of disabled persons, is not ava for those in the older age groups  Of the 911 di persons who were over the age of 45, the difficu finding a suitable job had prevented resettlement in as compared with 5% of those who were under 45 wastage of man-power over the age of 40 in this co is not fully appreciated and it is increasing  So lo it continues, difficulties must arise in the resettlem the disabled in the same age group  The greatest e at rehabilitation have been made for the young di persons from whom the greatest returns can be exp the problems of the over 40s loom up ominously

### Pathology of Rehabilitation

In assessing the influences that hinder resettle it was found that while the pattern of every case v one or more of four fundamental factors were alwa cause of difficulty in resettlement  (1) psycholo factors, (2) physical disability, (3) lack of su



Incidence of factors that chiefly hinder resettlement at different

E II—THE EMPLOYMENT STATE, THE EMPLOYABILITY AND THE CAUSES OF FAILURE TO BECOME RESETTLED IN CERTAIN DISEASE GROUPS

| Disease group | Employment state (%) | | | Employability % | | | | Cause of failure to become resettled % due to | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | Satisfactorily employed | Unsatisfactorily employed | Unemployed | Grade I | Grade II | Grade III | Grade IV | Physical factors | Psychological factors | Failure to rehabilitate | No suitable job |
| hiatric disease | 46 | 9 | 45 | 11 | 57 | 21 | 11 | 6 | 70 | 2 | 3 |
| rthritis | 43 | 7 | 50 | 6 | 51 | 33 | 10 | 48 | 24 | 3 | 10 |
| psy | 47 | 6 | 47 | 10 | 52 | 35 | 3 | 35 | 47 | 8 | 5 |
| onary tuberculosis | 45 | 11 | 44 | 10 | 62 | 17 | 11 | 46 | 4 | 4 | 15 |
| c ulcer | 60 | 7 | 33 | 15 | 68 | 8 | 9 | 21 | 28 | 5 | 7 |
| ovascular disease | 39 | 5 | 56 | 13 | 43 | 31 | 13 | 39 | 29 | 2 | 11 |
| matic disease | 53 | 6 | 40 | 14 | 58 | 22 | 6 | 39 | 12 | 3 | 17 |
| etes mellitus | 45 | 10 | 45 | 20 | 60 | 15 | 5 | 35 | 15 | 10 | 5 |

k and (4) misuse or disuse of existing methods of bilitation

psychological factor hinders resettlement more often a physical disability until the 45–50 age group is ed (see figure) After the age of 50 psychological ors play a subsidiary rôle in preventing resettlement physical disabilities are dominant The difficulty in ing suitable work increases with age and is a potent or in preventing resettlement in the older age groups

## PSYCHOLOGICAL FACTORS

this sample 212 (10 4%) were registered with a nosis of psychiatric disease but a further 284 6%) with a diagnosis of organic disease were affected psychological factors hindering their resettlement se two groups—the ‘ open and the ‘ masked hiatric cases—thus represent a quarter of all the bled persons seen.

### Psychiatric Group

f the 212 recognised as having a psychological dis ity most had chronic anxiety states dating from a rious unpleasant experience (such as war service or anic illness with hysterical perpetuation of symptoms) ad family history of mental breakdown was common not the rule Many of these people would never have eloped symptoms but for the unusual conditions of es to which they were subjected Few had received chiatric treatment. The commonest diagnosis with h they were registered was neurasthenia Employ t state, employability and the causes of failure to ome resettled are shown in table II Paradoxically these 212 persons registered because of a psychiatric ase had an organic disability which prevented ttlement.

### ked Psychiatric Group

D R.O.s have gained the impression that a high propor n of persons labelled as having organic disease are abled by neurotic symptoms They are powerless separate these cases or to give the neurotic person the damental help he needs Their impression is amply rmed by this survey in which 14 6% of all the abled persons seen had been registered for an organic ase although resettlement was hindered by a chiatric disability

Most of those with a marked neurosis develop their psychi ic symptoms after completion of hospital treatment when ey are attempting to return to a normal way of life Neurotic mptoms do not develop while active treatment in which ey have faith is being carried out in a modern hospital with its trappings and powers of suggestion On registration disabled person with his label of organic disease takes his a disability card from employer to employer At this he has already been discharged from the hospital or and the anxiety symptoms which he accepts as part of disability flourish unchecked D R O.s hesitate to recom d him, for if an employer accepts a disabled person who later found to be an unsatisfactory employee he is likely be less coöperative about the next disabled person offered to him Many employers are no less observant than D.R O.s, and avoid this type of neurotic workman

While many mentally unstable persons especially those with obsessional tendencies, make good employees and may be outstandingly successful, those with hysterical perpetuation of symptoms following organic disease have difficulty in becoming resettled Of the 284 masked psychiatric cases, 60% were out of work and suffering the added misery of being unemployed in a time of full employment Most of them were no longer under medical care at the time of interview

The neurosis associated with organic disease and especi ally the compensation neurosis would benefit from early simple psychotherapy in the form of explanation The well meant advice of friends and even doctors has often fostered compensation neurosis, of which there were 32 cases in this group

### Unclassified Neurosis

Of the 284 cases 21 who were not prevented from being resettled by any organic disorders (though they were registered on account of such disorders) were grouped together as having an ‘ unclassified neurosis D R.O.s the most experienced people in contact with this group would label them as malingerers or work shy Certainly they comprise the poor human material often found in common lodging houses but to call them work-shy is to pass moral judgment The description by Maughs (1940) of the psychopath describes most nearly the majority of this group

> The *psychopath* in contrast to the *psychotic* is fully aware of society and his fellow men and cannot be declared legally insane In this sense he resembles the neurotic but is far more likely to commit crimes and is rarely troubled by the pangs of conscience A psychopath usually lacks sympathy fails to recognise the rights and feelings of others and i predominantly a predatory person

The quantitative importance of these cases is not reflected by the figure of 21 (out of 1045) found in this study since 15% of the cases selected for interview were never seen Most of this 15% had given temporary doss house ’ addresses Such people rarely seek medical advice and their prognosis as regards rehabilitation appears hopeless A study of hostel life might throw light on the ætiology and perpetuating factors of these problem cases

## PHYSICAL DISABILITIES

Orthopædic and traumatic conditions are mainly static and resettlement once achieved is likely to be permanent Hence rehabilitation has been most success ful in such cases, in contrast with the fluctuating medical disabilities where the difficulties of rehabilitation are formidable Employers show more sympathy for those with obvious traumatic disabilities especially if incurred during war service than they do to those with humdrum conditions such as bronchitis Of the medically disabled 48% were unemployed as compared with 32% of the surgically disabled Medical disabilities are not only more difficult to rehabilitate but are twice as com

Analysis has therefore been confined to certain medical disabilities

Whatever the cause of disability the employment state and the severity of the disease, as assessed by employability, was remarkably similar in the different disease groups (table II) This suggests that the resettlement of a person depends not so much on the disease itself but on other factors Causes of failure to become resettled, however, do show some striking differences Naturally psychological factors prevent resettlement of those with psychiatric disease, and mental disabilities affect the rehabilitation of some epileptic persons, but there are also less expected differences Thus the incidence of psychological factors affecting resettlement is six times as great for bronchitis as for pulmonary tuberculosis, and a far higher proportion of persons with peptic ulcers and heart disease are hampered by psychological symptoms than are people with rheumatic disease

*Bronchitis Group*

Bronchitis, the highest single medical cause of registration accounted for 8% of the registered disabled persons The proportion unemployed was only exceeded by the group with cardiovascular disease Although 33% were fit only for sheltered work, none had been placed in Remploy factories or designated work, although many had been placed by employers in the equivalent of sheltered work

Employers often fail to tolerate the long sick absences of these workers during exacerbations of their disease, and fit fellow workers may resent doing the heavy jobs for the man with a cough There is no doubt that places are being taken in Remploy factories by persons more fitted for open competitive work than the sufferer from bronchitis *The necessity for sheltered work of the Remploy factory type is greater for this disability than any others except epilepsy and pulmonary tuberculosis* For the last two conditions, the need has been recognised if not fully met, yet there are nearly as many people registered as disabled with bronchitis as with pulmonary tuberculosis and epilepsy together

*Epilepsy*

In this sample 3% were suffering from epilepsy There has been overemphasis of the danger of employing epileptic persons in industry Each case must be judged on its own merits Only 1 of the 33 employed cases was in work that was medically unsuitable, and of the 62 cases only 2 were unemployable, yet it has often been thought that a high proportion of persons suffering from this disease are unfitted for any work The Ministry of Labour (1947) has circulated among employers a restrained and fair case for the employment of epileptic persons

The fear of employing epileptics has resulted in the real danger of the disability being concealed One man was also registered for flat feet, and only mentioned this when employers asked on what grounds he was registered as disabled Another told how he was able to get into the lavatory before he had his grand-mal attacks Persons with epilepsy stated that they had fewer attacks when happily employed and that unemployment increased the frequency of fits

*Pulmonary Tuberculosis*

The incidence of pulmonary tuberculosis was 5% This disease, together with the psychological disorders and epilepsy, is the main cause of disability in the younger age groups In no other medical condition is the resettlement of the patient so automatically considered as a routine part of the treatment

Of these cases, 77% were still attending chest clinics at the time of the interview At the long follow up by chest clinics definite instructions regarding work were given (in contrast to the vague advice given in many general medical outpatient departments), and close coöperation between D R O.s and chest physicians made it possible for these instructions to be carried out as far as possible Even so, only 6% of those suffering from pulmonary tuberculosis were doing part-time work, and a far higher proportion (15%) than in the other disease groups were being hindered in resettlement by lack of

The danger of spread of infection at work, which is to be greatest in unsuspected cases, has not been fully ated, but it is a potent reason for the extension of P factories for tuberculous persons

*Peptic Ulcer*

Hurst and Stewart (1929) found evidence of p ulceration in 10% of post-mortem cases The incid in this survey was 6 8% Of the 122 persons with disease, 57 were between the ages of 35 and 50 Fr table II it will be seen that peptic ulcer is the only c tion in which psychological factors play a more impor part than the organic disease itself in preventing res ment The degree to which this condition affects employability of the industrial worker is shown by D survey (1949) of time lost by peptic ulcer patients

*Cardiovascular Disease*

There were 115 persons disabled with cardiova disease (5 9% of the total) Hypertension and dege tive heart-disease were common, but there were paratively few cases of rheumatic heart-disease. with so called valvular heart disease had benign systolic murmurs There were a number with car neurosis and no evidence of organic disease who unemployed

Of the unemployed cases, one of the most unfortunate a young man who had had a good job as a bank clerk He found on routine examination to have mitral stenosis, therefore lost his job He had enjoyed his work and rem symptom free until the diagnosis was made Since that he had developed an anxiety state about his heart cond which made his placing in suitable work very difficult

The essential need for the adolescent person heart disease is sufficient education and training enable him to do suitable sedentary work

*Chronic Rheumatic Diseases*

This group of diseases, with chronic bronchitis cardiovascular disease, is the main cause of disability the elderly Despite severe crippling in this group, employment state compared favourably with that in groups suffering from bronchitis and heart disease was clearly related to the comparative freedom f anxiety states in most of those suffering from rheum disease

*Diabetes Mellitus*

There were only 20 disabled persons (just 1%) diabetes mellitus in this survey The incidence is because with modern treatment the person with unc plicated diabetes should not need the benefits of Disabled Persons Act

## Difficulties in Finding Suitable Work

For 169 of the disabled persons seen employment w would have been suitable was not available The q system is designed to prevent fluctuations of employm from affecting the security of disabled persons in indust Yet this survey, done at a time of nearly full emp ment, shows that 8% of the disabled persons could find a suitable job, and the quota system could prevent their unemployment figure from rising

68 (40%) of this group of 169 persons for whom suitab work could not be found, were fit for sheltered employ ment only, for the whole survey, the correspondin percentage was only 19 This emphasises the need for greater facilities for sheltered work than exists at present In the whole survey 1035 (53%) were considered fit fo open competitive work

In London and many parts of the south-east of Eng a wide selection of light work is available, mainly in firms It is possible to place a high proportion of disab persons in this type of open competitive work Heavy indus unsuitable for the employment of many disabled persons run by large organisations Nevertheless, where the ch lies between a large or a small organisation, other things b al the large organisation should be chosen, since a small may unexpectedly close down

lthough light industry must absorb the greatest number isabled persons in this country, it is possible for heavy and ium industry to share in this responsibility Vauxhall ors Ltd employs many of its own disabled persons (Plowes l 1948)

f the 169 for whom resettlement was hindered by k of suitable work, 24% had served an apprenticeship period of training before becoming disabled For survey as a whole 22% had served an apprenticeship some sort. Apprenticeship and years in some heavy k had often made it especially difficult for a person become adapted to a light job after becoming disd In this group of 169, 23 (14%) had had occupa al training as disabled persons—mainly in Govern nt training centres In the survey as a whole 12% had training after becoming disabled

hen a disabled person had been sent to a Government ning centre a course of training suitable for his disability generally been chosen; but after training it had some es been impossible to place them in work. One had regis d because of chronic otitis media and had done a course ualify as a sanitary inspector He had since been short d for a suitable post and rejected on medical grounds use of his ear condition. When interviewed he was still mployed.

### Misuse and Disuse of Existing Methods

n 75 cases a man eager to work, fit for selected ployment, and with suitable work available was nd to be unemployed or employed in unsuitable work use or disuse of existing methods of rehabilitation apy had prevented resettlement Doctors D R O.s, ployers, and all others concerned with disabled persons st on occasions have failed to give them the help y needed

ometimes his doctor's assessment of a man's case has led to suppose himself weaker than he is sometimes a man not been supplied with a piece of necessary equipment h as an electrically propelled wheelchair) sometimes t work has been prescribed for a trivial and passing com int and the man has taken it as an injunction never to do y work again Sometimes patients with rheumatism hma, or other chronic medical diseases have been told that locality in which they lived and worked was harmful their disease that they needed sea air They have given their employment disposed of their houses and moved with r families to the seaside Their disabilities have in many s worsened and the unemployment figures for disabled sons was high in these places.

There are many men in Remploy factories in the south-east England who have no right to be in sheltered work and o are blocking the entry of the severely disabled into mploy factories. A few of the 212 disabled persons who d undergone vocational training had been given wrong vice regarding the type of training thus a man with much uced vision was trained as a book-keeper and is still mployed Again employers may refuse to take back a n who is quite fit for his former work (e.g., a bank clerk h pulmonary tuberculosis controlled by artificial pneumo rax and 2 others with mild heart disease)

### Summary

A study has been made of 1945 disabled persons seen the south-east of England

Of these 36% were unemployed and of the 64% who re employed 15% were in work that was unsatisfac y The work was unsatisfactory on socio-economic ounds and only rarely for medical reasons

The quota system can never be fully effective until re stringent criteria are applied for the registration disabled persons In this survey 20% of the disabled sons had disabilities which did not substantially ndicap them in finding or keeping employment to ich they were suited

Provisions for sheltered work in the south-east of gland were found to be inadequate Of those that were substantially handicapped 70% were fit for selected open competitive work and 30% needed sheltered work There was no suitable work available for 18% of the latter group

Four main factors had prevented resettlement

1 A psychological factor (the predominant cause of failure in disabled persons under the age of 45)
2 Physical disability (of greater importance in the older age groups)
3 Lack of suitable work for those requiring sheltered working conditions
4 Misuse and disuse of existing methods of rehabilitation.

Resettlement of those disabled by medical conditions is far more difficult than resettlement of those with a static disability resulting from injury A more detailed analysis was therefore made of the disabled persons who had chronic medical diseases

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## ARTERIOGRAPHIC APPEARANCES OF THE DIGITAL ARTERIES OF THE HANDS IN RAYNAUD'S DISEASE

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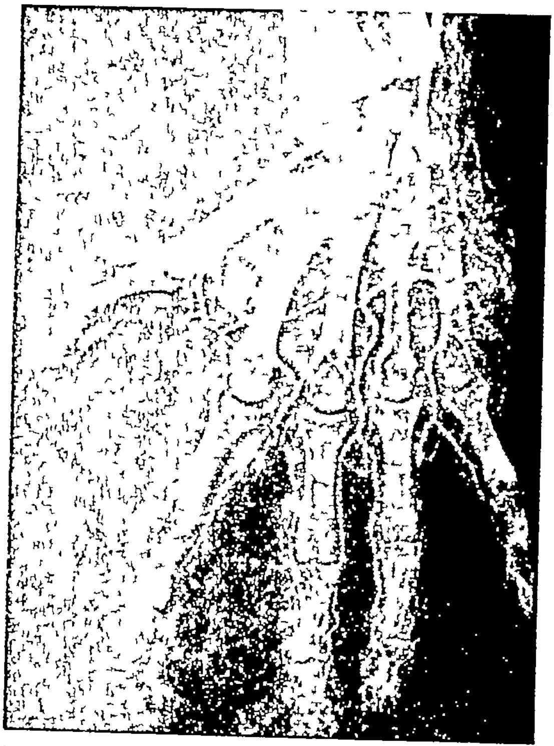
No abnormality of the peripheral circulation has been the subject of more controversy than intermittent spasm of the digital arteries associated with colour changes —so-called Raynaud's disease There is an important reason for the confusion which surrounds the condition Whereas it was originally assumed that the patients described by Raynaud formed a homologous group they were in fact a varied collection Such a misconception would not have arisen to be perpetuated if it had been more fully appreciated that the major purpose of Raynaud's (1888) thesis was to show that not all cases of colour change were due to organic arterial disease since vascular spasm could by itself produce a similar clinical picture His original work included cases of scleroderma atherosclerosis and thrombo-angiitis obliterans and it has been the acceptance of all of these as Raynaud's disease that has been primarily responsible for the confusion which followed his work The name came to be so loosely applied that Hunt (1936) estimated that only about 30 of more than 600 published cases fulfilled the criteria laid down by Raynaud

Although Hutchinson (1901) had recognised that Raynaud's disease was not a single entity it was only with the classical investigations of Lewis and his colleagues (Lewis and Landis 1931 Lewis and Pickering 1934 Lewis 1938) that the existing confusion began to clear Lewis suggested the name Raynaud's phenomenon



ig 1—Woman aged 60 Arteriogram of left hand shows normal vascular pattern of palm and digits with very good circulation

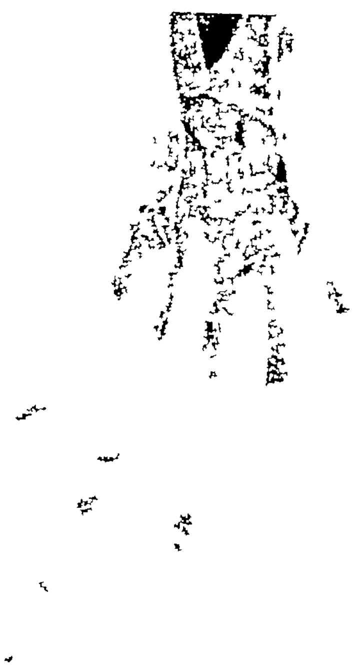


Fig 2—Woman aged 35 Arteriogram of right hand shows cir in hand and digits with distinct obliteration of nearly all arteries and inadequate circulation

to signify active and intermittent closure of small rteries of the order of those supplying the digits " He lso showed on clinical grounds that spasm could evelop in anatomically normal blood vessels or be ssociated with obstructive disease in the digital arteries hemselves

From the clinical response of some patients with aynaud's disease we suspected that obliteration of the igital arteries was a contra indication to sympathectomy e decided to exclude such patients from surgery by rteriographic demonstration of disease of the digital rteries

## Methods

23 patients were studied (14 women and 9 men) of ges ranging from 15 to 65 The proportion of men to omen in this small series corresponds to that found by ewis and Pickering (1934)

After the clinical data had been obtained, the bloodessels of both hands were studied by arteriography in e following manner

The patients were anæsthetised a blood pressure cuff was pplied round the arm well above the elbow, and the hand as then strapped firmly, but without constriction, to a ooden cassette tunnel The brachial tery at the elbow was entered by rcutaneous puncture At this stage e blood pressure cuff was inflated above systolic blood pressure to rest the arterial circulation in the nd 15 ml of 50% diodone was pidly injected, and the first film s exposed The circulation was nporarily restored by lowering the ssure in the cuff to diastolic level, d then the pressure was rapidly sed again and the second film was posed This was repeated until e films of the hand were obtained, whole procedure taking about seconds The opposite limb was ilarly examined There were no shaps ~~ mplications

## Results

Arteriography revealed two distinct groups of patien first, those in whom the digital arteries were anatomica normal (16 patients), and secondly those in whom digital arteries showed obliteration (7 patients)

In 1 patient with thrombo angiitis obliterans th was a partial block of one radial artery , in the remain 22 patients the radial and ulnar arteries and the pal arch showed no abnormalities

Representative examples of the arteriographic appe ances of the digital arteries of the hands in these t groups are shown in figs 1–4

The more important clinical data are summarised the accompanying table, which shows almost comp correlation between the arteriographic findings and nutritional state of the digits The patients show paronychial ulceration or infection, pulp atrophy, ridg brittle finger-nails, or phlyctenular gangrene were tha in whom arterial obliteration was demonstrable arteriography (figs 5–7) All 7 patients with clini evidence of ischæmic changes in the digits show arterial obliteration Of the 16 patients in whom arter

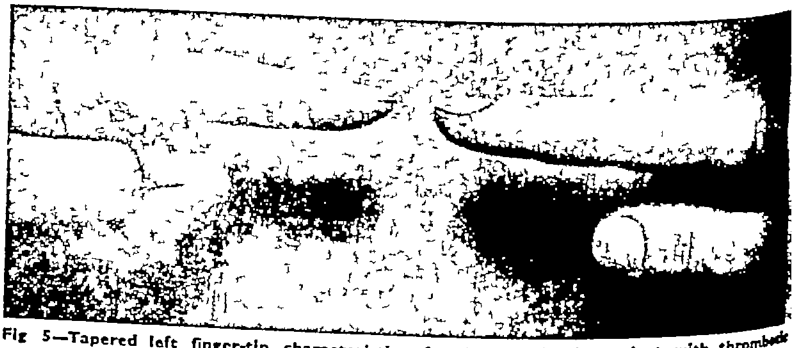
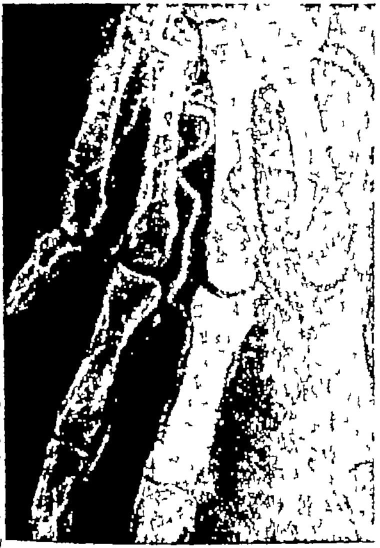


Fig 5—Tapered left finger-tip characteristic of pulp atrophy in patient with thromb digital-artery disease contrasted with the normal right side



3—Woman aged 41 Normal arteriogram of mid-carpus and proximal phalanges with very good circulation.

phy revealed normal digital arteries 15 showed no dence of impaired nutrition The single exception a girl aged 10, who had had severe chilblains all life and advanced acrocyanosis for five years She lately begun to have attacks of Raynaud s phenom n and got no relief from sympathectomy In spite eral atrophy the digital arteries although small

RESULTS OF ARTERIOGRAPHY

| t io-gram | No of cases | Age (yr ) | Sex |  | Dura tion of attacks (yr ) | Nutri tional changes | Systemic diseases |
|---|---|---|---|---|---|---|---|
|  |  |  | M | F |  |  |  |
| mal | 16 | 16–65 (av 35) | 6 | 10 | 1–30 (av 9) | 1 | Thrombo-angiitis obliterans (1 male) |
| ormal | 7 | 20–65 (av 50) | 3 | 4 | 0 5–4 (av [illegible]) | 7 | Thrombo-angiitis obliterans (1 male) |

owed no evidence of obliteration at the time of amination

A clinical diagnosis of thrombo angiitis obliterans was ade in 2 men (1 from each group) One other man th radiologically normal vessels had used a vibrating ol for many years.

Although the number of patients is small those with literation of the digital arteries were on the average 13 years older than those with radiologically normal ssels However, the duration of symptoms was more an four times as long in the patients with radiologically rmal digital arteries

The precipitating factor in all the cases was exposure cold and the character of the attacks was initially entical in both groups In the later stages of the sease the patients with obstruction of the digital teries had more frequent and more severe and persistent attacks with little relief even during warm weather In ntrast, the character of the attacks in patients with radiologically normal arteries had altered little over the years

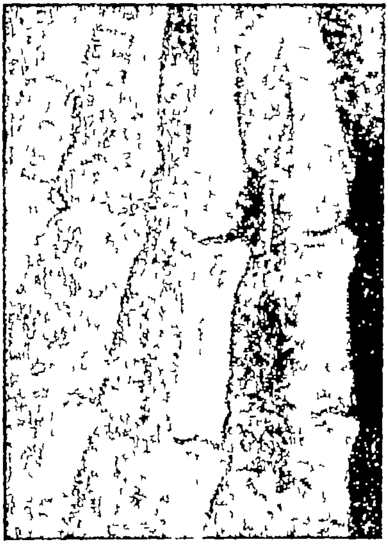


Fig 4—Man aged 60 Arteriogram of mid-carpus and proximal phalanges shows digital arteries to be blocked ; some collateral vessels have developed ; very inadequate circulation

## Discussion

The results of this study confirm that vascular spasm may develop not only in hands in which the digital arteries are structurally altered but also in hands in which the digital arteries are anatomically normal The correlation of clinical data with the arteriographic appearances supports the contention that uncomplicated vasoconstriction cannot be maintained sufficiently long to kill the skin (Lewis and Pickering 1934) In other words when nutritional changes develop in the fingers they are rarely caused by uncomplicated spasm of the arteries but are the result of structural occlusion thereof

It has not been proved that recurrent spasm of digital arteries can lead to structural changes which go on to thrombotic occlusion Such a sequence of events may

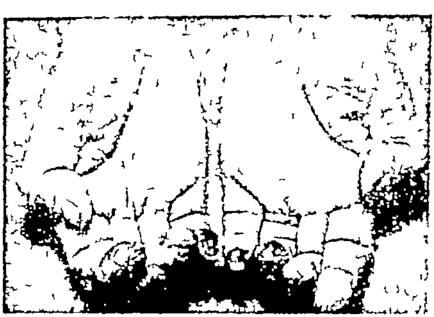


Fig 6—Woman aged 47 Acute necrosis of finger tips in thrombotic digital-artery disease

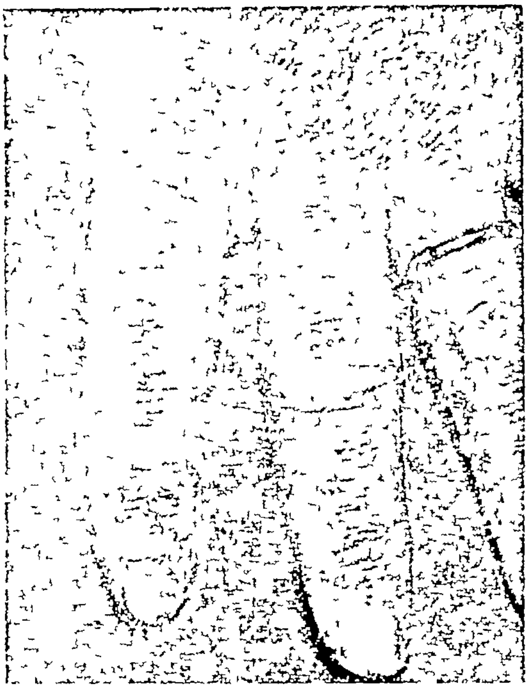


Fig 7—Same patient as in fig 2 ridged lustreless finger-nails and atrophied skin of finger-tips.

occur, but the fact that so few patients who have had intermittent spasm of the digital arteries for many years have nutritional changes suggests that it is rare No patient who has had attacks of spasm for more than five years in this study, and in a much larger group in whom arteriograms were not done, has yet developed nutritional changes A similar observation was made by Lewis The differences in age, duration of symptoms, tempo of progress, and arteriographic appearances suggest that there are two different conditions which present clinically with the same symptoms

The name of Raynaud should, we think, still be attached to recurrent attacks of symmetrical discoloration of the fingers, and sometimes the toes, due to intermittent *spasm of the digital arteries on exposure to cold*, but a distinction should be made between the patients in whom obliterative arterial changes are present and those in whom no anatomical abnormality can be demonstrated by arteriography We propose that the term Raynaud's phenomenon be retained for the latter group When obliteration of digital arteries can be demonstrated, the term "thrombotic digital artery disease" is preferable Perhaps Raynaud's disease would be a better name for this group, but it would cause confusion with existing usage

We have no histological evidence of the underlying pathology in the digital arteries of these patients, but such changes as do take place are non specific (Lewis 1938) This distinction is important in deciding treatment because the patient with Raynaud's phenomenon does well on treatment with vasodilator agents—e g, tolazoline—and sympathectomy, whereas in thrombotic digital-artery disease little can be done to improve the circulation, improvement following sympathectomy is slight, and early relapse is the rule Arteriography is a safe and satisfactory method of distinguishing between these two groups of patients

## Summary

Arteriograms of the digital arteries of the hands were made in 23 patients who had intermittent spasm and colour changes of the fingers

Two groups of patients emerged (1) those anatomically normal digital arteries, and (2) those wi obliteration of the digital arteries

These two groups are clinically separable, since th with digital-artery obliteration have nutritional chang in the fingers

The term Raynaud's phenomenon should be retained designate intermittent spasm of the digital arte without clinical complication and with a normal arte graphic appearance of the digital arteries

"Thrombotic digital-artery disease" is a better when local nutritional changes are present and ther arteriographic evidence of obliteration of the arteries

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# NEUROPATHY IN DIABETES MELLITU

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NEUROPATHY is common in diabetes mellitus, and complication has proved common during routine exam tions of diabetic patients attending the dietetic patient department of the Royal Infirmary, Edinbu I correlate here the incidence of neuropathy with age of the patient, the duration, severity, and contr the diabetes, and the coexistence of vascular disease

## Criteria and Material

Neuropathy was taken as present when unequiv signs of neurone damage were found on a limited ne logical examination Neuritic symptoms without were disregarded in this assessment The examinat included tests for reflex activity, gross muscle weak well marked hyperæsthesia, and loss of sensation vibration, position, pinprick, and light touch S depression of the reflexes and mild changes in sens were not accepted for the purpose of this study S of neuropathy were found in 37% of 545 diabetics

## Results

### *Age*

The patient's age at the time of examination recorded in one of seven groups less than 20, 20 30–39, 40–49, 50–59, 60–69, and 70 or more It is known that senile degeneration affects the neurone non diabetics aged more than 50, so a compara study of loss of knee and ankle reflexes and vibra sense in the legs in 574 non diabetic patients aged than 50 was made Table I shows that after the ag 50 the incidence of neuropathy is higher in diab than in non-diabetic patients and increases with but between the ages of 20 and 60 the incidence incre

TABLE I—AGE INCIDENCE OF NEUROPATHY

| Age (yr) | Diabetics | | Non-diabetics | |
|---|---|---|---|---|
| | Total no | Percentage with neuropathy | Total no | Percent with neurop |
| Under 20 | 29 | 10 | | |
| 20–29 | 50 | 22 | | |
| 30–39 | 59 | 24 | | |
| 40–49 | 82 | 33 | | |
| 50–59 | 110 | 31 | 341 | 5 |
| 60–69 | 143 | 52 | 162 | 25 |
| 70 or over | 72 | 55 | 71 | 41 |

TABLE II—NEUROPATHY AND SEVERITY OF DIABETES

| Grade of diabetes | Total no | Percentage with neuropathy |
|---|---|---|
| *der age 50* | | |
| ild (diet only) | 31 | 10 |
| edium (insulin 0–50 units per day) | 10 | 25 |
| evere (insulin over 50 units per day) | 82 | 30 |
| *r age 50* | | |
| ild (diet only) | 139 | 32 |
| edium (insulin 0–50 units per day) | 104 | 55 |
| evere (insulin over 50 units per day) | [illegible] | 50 |

only 11% This comparison of the incidence of neuro thy in the diabetic and non diabetic groups was not etly valid because the examination for signs in the vous system was more complete in the diabetics re than 90% of the diabetics however had loss of lexes or vibration sense in the legs; so the comparison reasonable Since an appreciable number of non betics aged more than 50 have signs of neuropathy figures representing severity, duration and control of betes have been separated into two groups over and der the age of 50

*erity*

The patients have been divided into three grades ording to the severity of diabetes (1) mild in ich a weighed diet alone was required for diabetic trol; (2) "medium" in which insulin up to a total age of 50 units in the day was required as well as a ghed diet and (3) "severe" in which 50 units or re of insulin was required in the day as well as a ghed diet. Table II shows that neuropathy is more mmon among those who require insulin but mild betics even aged less than 50 can develop neuropathy

*ration*

Table III shows the incidence of neuropathy with the ation of diabetes Under the age of 50 44% of 72 ients who had had diabetes for ten years or more had ns of neuropathy, whereas 15% of 148 patients who d had diabetes for less than ten years had signs of uropathy In the elderly diabetics neuropathy was en the presenting feature and it is well known that onset of diabetes may precede this sometimes by ny years Thus the significance of duration of diabetes relation to neuropathy may be in the length of time at a patient has been in a state of uncontrolled diabetes

TABLE III—NEUROPATHY AND DURATION OF DIABETES

| Duration (yr) | Total no | Percentage with neuropathy |
|---|---|---|
| *der age 50* | | |
| nder 5 | 101 | 14 |
| –9 | 47 | 19 |
| –14 | 39 | 41 |
| 5 or over | 33 | 45 |
| *r age 50* | | |
| nder 5 | 151 | 37 |
| 5–9 | 76 | 45 |
| 10–14 | 46 | 63 |
| 5 or over | 32 | 58 |

*ontrol*

Two categories of control have been used— fair nd poor Patients have been placed in the poor tegory if any of the following symptoms or signs have en observed thirst polyuria or nocturia over continu us periods of four weeks or more at any time after the itial period of treatment ketosis over a similar period f time or persistent glycosuria + + or more with the uantitative Fehling's test Loss of weight often drew attention to poor control and was usually associated with ent glycosuria Patients were also placed in the poor category if they had defaulted from attending the clinic for longer than six months 237 patients had poor control and neuropathy had developed in 64% of these In contrast only 17% of 308 patients with fair control had neuropathy Table IV presents the relationship of control to the incidence of neuropathy according to age and duration It can be seen clearly that whatever the age of the patient or the duration of the diabetes neuropathy developed much more often among those with poor control Under the age of 50 when senile neuropathy is unlikely, only 5% of 115 patients with fair control had neuropathy On the other hand, neuropathy was found in 47% of 105 patients aged less than 50 with poor control

*Vascular Disease*

Vascular disease was regarded as present in both diabetic and non-diabetic patients if any of the following conditions were found (1) a diastolic blood pressure above 90 mm Hg (2) palpable thickening and tortuosity in any of the blood vessels of the arms or legs (3) a history of angina of effort myocardial infarction, or intermittent claudication and (4) atherosclerosis in the retinal arterioles In diabetic patients the additional features of retinopathy and albuminuria were also taken as evidence of vascular disease Table V shows that the incidence of neuropathy was higher in diabetics aged more than 50 with vascular disease than in a comparable group of non diabetics with vascular disease

TABLE IV—NEUROPATHY AND CONTROL OF DIABETES

| Duration (yr) and age group | Fair control | | Poor control | |
|---|---|---|---|---|
| | Total no | Percentage with neuropathy | Total no | Percentage with neuropathy |
| *Duration less than 10* | | | | |
| Under age 50 | 87 | 5 | 61 | 31 |
| Over age 50 | 148 | [illegible] | 79 | 73 |
| *Duration more than 10* | | | | |
| Under age 50 | 28 | 11 | 44 | 64 |
| Over age 50 | 45 | 31 | 53 | 85 |
| Total | 308 | 17 | [illegible] | 64 |

## Discussion

It is clear from these figures that adequate control of the diabetes is the most important factor in the prevention of neuropathy This is the established view of many other workers In this series there were 55 patients aged less than 50 in whom senile neuropathy was unlikely to have been present and 80% had been poorly controlled This figure may be more significant than those in table IV which shows the incidence of neuropathy among poorly controlled diabetics because many of these patients may have had signs of neuropathy from which they had recovered by the time they were examined Moreover I have not included symptoms and there must be few diabetic patients who have not experienced pains or paræsthesiæ at some time or other nearly always when control is inadequate—for example at the onset of the diabetes It is a common finding also that these

TABLE V—NEUROPATHY AND VASCULAR DISEASE

| Age (yr) | Vascular disease | | | |
|---|---|---|---|---|
| | Diabetics | | Non-diabetics | |
| | Total no | Percentage with neuropathy | Total no | Percentage with neuropathy |
| 50–59 | 69 | [illegible] | [illegible] | 17 |
| 60–69 | 114 | [illegible] | [illegible] | 40 |
| 70 or over | 63 | [illegible] | [illegible] | [illegible] |

symptoms disappear when the diabetes is carefully controlled It is striking that only 5% of 115 patients aged less than 50 with "fair" control had neuropathy This is well within the bounds of error in the rather loose assessment of control used here, and it is extremely probable that diabetic neuropathy hardly ever occurs in the well controlled patient

However, the contention that poor control of the diabetes is the direct and only factor concerned in the development of neuropathy is more difficult to substantiate than the fact of its importance

The rôle of deficiency of vitamin $B_1$ in the ætiology of diabetic neuropathy has been the subject of much dispute The similarity of the neuritis of diabetes to that of alcoholism or beriberi is suggestive, but the fact that diabetic neuropathy does not respond to vitamin B is now well established (Rundles 1945, Broch and Klovstad 1947, Hirson et al 1953) and has been repeatedly proved in patients from this clinic In this respect it is interesting that studies of pyruvic acid metabolism, which is disturbed in vitamin B deficiency, have not shown any such disturbance in diabetic neuropathy (Martin 1953)

Certain workers—e g, Jordan (1936) and Broch and Klovstad (1947)—have commented on the association of vascular disease with neuropathy in diabetes Examination of the nerves in limbs amputated for gangrene in diabetes has shown neurone degeneration with obliterative vascular disease of the vasa nervorum (Woltman and Wilder 1929), and necrosis of the vasa nervorum with periarteritis nodosa can cause a neuropathy which is very similar to that found in diabetes (Heathfield and Williams 1954)

There are, however, good arguments against the view that vascular disease is concerned in the causation of diabetic neuropathy The much higher incidence of neuropathy in diabetics compared with non diabetics with vascular disease suggests that another factor is involved Martin (1953) studied the peripheral blood flow in patients with diabetic neuropathy and showed that neuropathy may develop in the presence of a good circulation Moreover it is significant that 42% of 55 diabetics aged less than 50 with neuropathy had no evidence of vascular disease according to the criteria used here It is remarkable, too, that only 40% of the 204 patients with neuropathy had diabetic retinopathy or albuminuria, which suggests that diabetic angiopathy does not involve the vasa nervorum in the same way as the vessels of the retina and kidney Furthermore recovery from neuropathy, particularly from neuritic symptoms, with control of the diabetes is common, and up to now vascular disease has been regarded as irreversible Thus it is probable that the mechanisms involved in the development of vascular disease and neuropathy are different, but that both have their origin in the metabolic disorders present in the poorly controlled diabetic

It is believed that the degree of control can be most readily assessed by the presence or absence of glycosuria, which is evidence of hyperglycæmia outside the physiological normal, except where a low renal threshold for glucose has been proved The aim of good control in diabetes is to achieve normoglycæmia with sugar free urine, so far as possible, for this purpose an accurate diet as well as careful insulin cover is desirable Such accuracy is useful in preventing complications in diabetes, particularly neuropathy

## Summary

Signs of neuropathy were found in 37% of 545 diabetics

The incidence of neuropathy was related to the patient's age the duration severity, and control of the diabetes, and the coexistence of vascular disease

Poor control is the most important factor in the development of neuropathy in diabetes 64% of 237 patients with poor control had neuropathy, wherea 17% of 308 patients with fair control had neuropath and 89% of 55 patients aged less than 50 with neu pathy, in whom senile neuropathy was unlikely to present, had been poorly controlled

Arguments are put forward to show that neuropa in diabetics is not caused by vitamin $B_1$ deficiency or vascular disease of the vasa nervorum The neuropa is probably due to the disordered metabolism pres diabetes

I am indebted to Prof D M Dunlop for his con encouragement and advice, and Sister A. Buchan, Sister *Cameron and the staffs of the dietetic and medical* patient departments of the Royal Infirmary, Edinburgh, their help

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# HYDROCORTISONE IN LESIONS OF SO TISSUE

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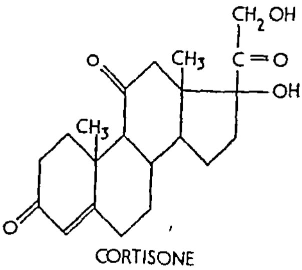
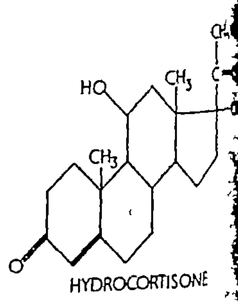
Hydrocortisone (17-hydroxycorticosterone), a ph ologically active adrenocortical steroid was origi isolated by E C Kendall in 1940 and called Compoun to distinguish it from cortisone, which was known Compound E



CORTISONE



HYDROCORTISONE

Originally it was used (Fourman et al 1950) as a parent antirheumatic agent, when it was found to have sim properties to cortisone Hollander et al (1951), howe showed that it was at least four times as active cortisone when the acetate salt was injected locally a suspension

Hollander et al described it as having considerable lo "anti inflammatory and anti fibrinolytic" activity, reported a high percentage of successes in a consider series of intra articular injections for rheumatoid arthritis and osteo arthritis

Boland (1952) obtained almost identical results

Hydrocortisone has since been investigated in thi country as an intra articular antirheumatic agent by many workers, most of whom have had far less favour able results and point out that, although the active inflammation within the joint normally responds readily to hydrocortisone, relapse follows within a relatively short period and frequent reinjection becomes necessary with the subsequent risk of injury to the joint

Hydrocortisone seems to be of far greater value in conditions which are essentially reversible without ndency to relapse This has indeed proved to be the se

Hollander et al (1951 1953a and b) and Boland (195–) their original and subsequent reports mention several cases soft-tissue lesions—e g periarthritis of the shoulder and cranon bursitis—which responded favourably to local ection of hydrocortisone

In this country Murley (1954) and Quinn and Binks (1954) port good results in tennis elbow whereas Freeland and ble (1954) suggest that hydrocortisone is no more effective an 5% procaine injection

Robecchi and Capra (1953) in Turin obtained excellent ults in both acute and chronic periarthritis of the shoulder nt whereas Cyriax and Troisier (1953) in London reported or results in freezing arthritis' of the shoulder

The present series of 208 cases treated with hydro tisone injection represents almost a full year's trial this form of treatment for the several types of soft sue rheumatism' commonly observed in normal ctice Tennis elbow (lateral epicondylitis) and golfer's ow (medial epicondylitis) plantar fasciitis, olecranon d prepatellar bursitis and the various acute and ronic soft tissue lesions of the shoulder joint are all mmon conditions in which trauma is supposedly lowed by low grade non specific inflammation The ential lesion is in doubt but the general picture con ts in local pain, tenderness, and œdema of the soft sues with the formation of adhesions and limitation movement. Such cases are essentially reversible when ated, and do not tend to relapse once they have covered. They therefore seem to be ideally suited to atment with hydrocortisone A similar response to uma is seen in the synovial membranes of joints in ich local inflammation, shown by acute effusion lows the injury and can be considered to be a reaction the soft tissues to it As such it should also respond hydrocortisone

Although these conditions have a natural history of ontaneous recovery the period of painful incapacity is ten long and the patient often receives much unavailing ysiotherapy Any treatment which can reduce the ration of the disability and the amount of other atment required would be of great value to practi oners and hospital departments alike

## Technique

Hydrocortisone acetate was used throughout the ries and with very few exceptions the dose was 25 mg a 1 ml. suspension

The main difficulty in treating lesions of the soft tissues s always been accurate localisation of the lesion The one affected is often widespread making the above entioned dose of hydrocortisone seem too small for equate dispersal and contact Moreover hydrocortisone only slightly soluble in plasma Therefore to help read the hydrocortisone through the tissues the spension was mixed with hyaluronidase 1000 units ssolved in 2–5 ml of 2% procaine hydrochloride The vantages of this mixture are fourfold (1) it provides more manageable quantity of solution (2) its local aesthetic action confirms accurate localisation (3) it ves the patient immediate relief and (4) the hyalu onidase ensures the greatest local dispersion of the suspension.

The fluid was injected directly into the site of greatest local tenderness determined by palpation and resisted movement and the *needle was moved around the site* during injection This technique was not always possible in dealing with joints, so the following variations were practised

In the shoulder joint if it was found difficult to identify the region of the lesion the injection was given anteriorly into the subacromial bursa and laterally into the area of the long head of the biceps muscle; occasionally a third injection was given posteriorly into the region of the capsule of the joint

Joints treated for acute effusion were injected with hydrocortisone and hyaluronidase alone (Kendall 1954) The method of approaching the joint in such cases was left to individual preference

No dressing or splinting was applied to the part after injection and the patient received no physiotherapy during the period of observation, although many had been referred after various periods of previous unsuccessful massage and exercises &c Most of the patients required one injection only, but several received repeated weekly injections when the primary condition showed only partial response to the first injection If after four such injections, total relief or considerable improvement was *not noted the treatment was considered to have failed* and was discontinued All the patients were treated as outpatients and were seen at twenty four hours seventy two hours one week two weeks and then at monthly intervals after the injections, independent opinions being sought so far as possible on the assessment of the result of each injection

## Results

Of 209 patients treated with 350 injections of hydro cortisone 176 *obtained complete or partial relief from* symptoms and 33 did *not* improve Recurrences were noted in 20 cases (about 10%) most of them within three months of treatment

### *Tennis Elbow and Golfer's Elbow*

Of 70 patients 50 obtained complete relief from pain and restoration of full function 7 made no improvement at all and 13 partially improved most of whom had sufficiently recovered after treatment to take up again their normal activities without any other form of therapy A persistent recurrence rate of 10% was observed 8 of the cases treated in this series relapsing within three months of injection So far the longest period between injections and recurrence in any one case has been two and a half months. Since the follow up of most of the cases has been for six to nine months we feel that further recurrences are unlikely

In almost every case the pain was worse after the immediate effect of the procaine had worn off and this lasted for thirty-six to seventy two hours After this reaction the symptoms gradually subsided usually being completely resolved within a week During this period of exacerbation the pain and tenderness seemed to be far more widespread than usual occasionally extending well above the elbow and down to the wrist

Results were occasionally dramatic

**Case 1**—A married woman, aged 36 had two years history of lateral epicondylitis which originally followed a long period of overtime using a guillotine After failure of physiotherapy a tenotomy of the extensor origin was done This did not relieve the symptoms. Three months after the operation an injection of hydrocortisone produced immediate relief and the symptoms never recurred Six months later the patient was still doing her normal work without any evidence of recurrence

TABLE I—RESPONSE OF SOFT TISSUE LESIONS TO HYDROCORTISONE INJECTION

| Diagnosis | No treated | Results | | | |
|---|---|---|---|---|---|
| | | Complete relief | Improved | No better | Recurrence |
| Tennis elbow | 59 | 40 | 10 | 6 | 8 |
| Golfer's elbow | 11 | 10 | 3 | 1 | – |
| Bursæ (olecranon and prepatellar) | 14 | 10 | 0 | 4 | 5 |
| Painful heels and plantar fasciitis | 10 | – | 1 | 8 | 3 |
| Tenosynovitis and trigger finger | 8 | 5 | 1 | – | 0 |
| Dupuytren's contracture | 6 | 4 | 1 | 1 | 0 |
| Myofascial tenderness | 20 | 11 | 3 | 3 | 1 |

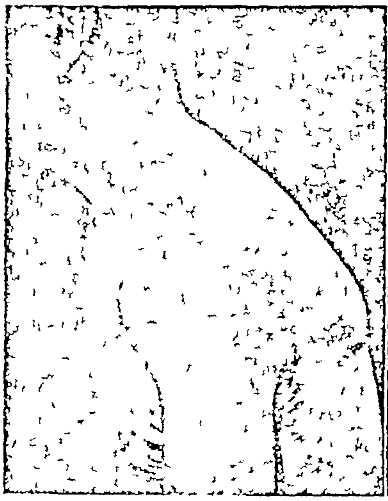


Fig 1

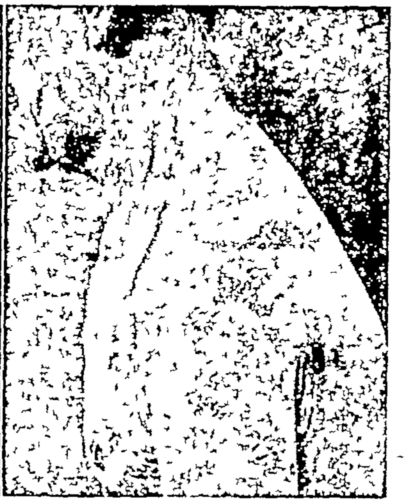


Fig 2

Fig 1—Case 2, showing gross distension of subacromial bursa before treatment.

Fig 2—Case 2 two weeks after one injection of hydrocortisone, procaine, and hyaluronidase No aspiration was done Swelling has completely subsided

*Lesions around Heel*

Of 19 patients with acute plantar fasciitis and pain in the heel 7 obtained complete relief and 8 did not improve, 1 of them apparently being made worse by the injection 3 of the successfully treated cases recurred within periods of up to four months and did not respond to a second course of injections Again an exacerbation of symptoms was noted after injection, and usually the worse the reaction the better was the result obtained

*Acute and Chronic Bursitis*

Of 14 bursæ injected 10 disappeared so dramatically as to be imperceptible seven to ten days later Of these, however, 8 recurred within varying periods of up to two months, and although they responded to further injections they invariably recurred

*Tenosynovitis, Trigger Finger, and Dupuytren's Contracture*

Relatively few cases of these conditions have so far been treated All 4 cases of trigger finger treated by the injection of hydrocortisone 12 5 mg into the tendon sheath recovered fully within a week

Of 6 patients with Dupuytren's contracture treated in the early stages 4 could fully extend the affected finger after treatment and 1 was partially improved These cases have, however, been followed up for only two months, although no further contracture has been noted in this short period

*Lesions of Shoulder joint*

It was often extremely difficult to determine which structure was responsible for the pain and stiffness in this joint At present diagnoses such as "supraspinatus strain" and "rotator cuff syndrome" hold pride of place with "periarthritis" and "capsulitis" Of 26 acute cases of the various types treated 14 were completely relieved, 10 were partly improved, and 2 showed no change

**Case 2**—A labourer, aged 68 had pain, stiffness and swelling of the left shoulder (fig 1) after "ricking" it work several days previously On examin the joint was grossly distended, and there much limitation of all movements. Hy- cortisone 25 mg was injected with proca and hyaluronidase, but no aspiration was do After two weeks the shoulder was normal size (fig 2), the patient was symptom-fr and his movements were almost full.

The typical response of an acute su spinatus tendonitis is well shown in fig.

In the chronic type of cases, us "chronic rotator cuff syndrome" "frozen shoulder" in type, the re have not been so good This is ha surprising, because such lesions, oc ring in late middle age, usually m the presence of a degenerative p cess Of 17 such cases treated progressed to complete recovery, improved to some extent, and 5 m no improvement whatever One cas "frozen shoulder," is worthy of note

**Case 3**—A married woman, aged had had for two years constant pain extreme stiffness of both shoulders wit apparent cause Routine physiotherapy had increased ra than diminished the symptoms Manipulation under ge anæsthesia produced no lasting response Hydrocort was accordingly injected into three points around the cap of each shoulder at weekly intervals Within four w abduction was almost full on both sides, and the patient put on to general shoulder exercises, by which means regained full range of movements

We have been most impressed by the frequency w which symptoms were relieved by injection into region of the long head of the biceps muscle as it lie the bicipital groove

**Case 4**—A man, aged 57, awoke one morning with se pain in his left shoulder By the following day the joint completely immobilised by protective muscle spasm, attempt at passive movement giving rise to agonising p Palpation revealed a point of extreme tenderness over long head of the biceps muscle, into which region hy cortisone was therefore injected Within eight hours patient was practically symptom free and a full ra of movement had returned He was not troubled by recurrence in the subsequent six months

*Acute Traumatic Effusions*

Treatment in these cases was reserved for joint which there was no bony or discrete ligamentous inj

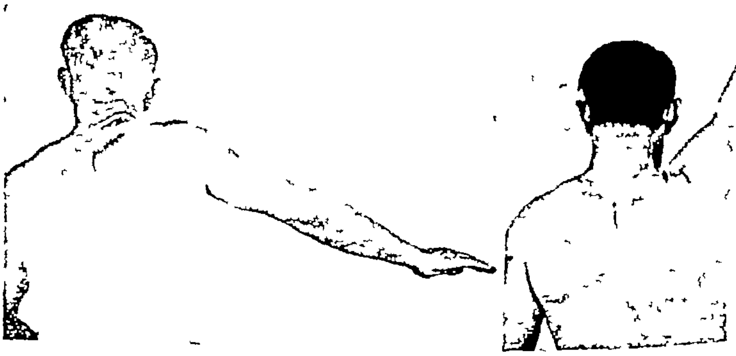


Fig 3—Man, aged 51 with acute supraspinatus tendinitis : *below* attempting abduction (note reversed scapulo-humeral rhythm) ; *to right* seven days after injection of hydrocortisone into point of greatest tenderness (abduction now almost full and scapulohumeral rhythm normal)

TABLE II—RESPONSE OF SOFT TISSUE JOINT LESIONS TO HYDROCORTISONE INJECTION

| Diagnosis | No treated | Results | | | |
|---|---|---|---|---|---|
| | | Complete relief | Improved | No better | R[illegible] |
| matic arthritis | 29 | 21 | 7 | 1 | 0 |
| lder l sions | | | | | |
| cute | 26 | 14 | 10 | [illegible] | 0 |
| ronic | 17 | 8 | 4 | 5 | 0 |

the 29 cases treated 21 responded very rapidly to drocortisone 7 were much improved and only 1 ained static In the successful cases the greatest ect was usually observed within seventy two hours

*ellaneous*

This group comprises the various muscular and ten ous lesions that are usually termed fibrositis or rofasciitis A clear-cut history of trauma is normally tainable, and tender indurated areas are easily able

f the 20 such cases treated 14 responded completely 3 did not change

*eral*

Only 1 case (of plantar fasciitis) was made worse by treatment, and only 1 case of local infection was erved, this case being of mild Dupuytren s contracture Despite a careful watch for the toxic effects usually ociated with cortisone none was observed presumably ause the doses are so relatively small The only toward reaction observed was transient urticaria lowing the injection of a knee joint.

## Discussion

Hydrocortisone has proved most effective in the atment of lesions of the soft tissues It is without estion the treatment of choice in tennis elbow and ller s elbow reducing the treatment to one or two ekly injections and eliminating in most cases the long riods of physical treatment otherwise required

In the treatment of recent intra articular and peri ticular injuries of the soft tissues hydrocortisone is uable in hastening recovery which otherwise is en protracted It has a wide sphere of application, rticularly in association with the careful combined e of non weight-bearing exercises of the injured rt.

Most of the acute shoulder lesions responded dramatic lly to local injections of hydrocortisone, and we feel at this substance should be tried in every acute se

In the more chronic type of shoulder disability cluding the " freezing arthritis mentioned by Cyriax d Troisier (1953) as not responding to hydrocortisone r results were not so successful as in the acute cases t the fact that we were successful in 48% of chronic ses suggests that hydrocortisone should be tried Many of the patients who do not obtain complete relief have either increased range of movement or less pain Several patients who had completely ' frozen shoulders which responded to no form of physiotherapy made rapid progress when given the same treatment after hydrocortisone injections even though hydrocortisone by itself did not produce any detectable response

The few cases of tenosynovitis and trigger finger treated showed a good response to hydrocortisone such cases are probably well worth a trial injection before being submitted to long periods of splinting or to surgery

The response of plantar fasciitis was particularly dis appointing the proportion of successful results being rather less than 40% Although this lesion appears to be ideally suited to hydrocortisone injection results have not been so good as anticipated The probable reason for this is the difficulty in locating exactly the site of the inflammation within the fascial planes—if there is one In view of the difficulty of treating this condition by other methods however it is again prob ably worth while observing the effect of hydrocortisone before proceeding with them

The immediate response of acute prepatellar bursitis and olecranon bursitis is normally complete rapid resolution of inflammation and diminution of the bursa After periods varying from seven days to three months, however a high percentage of the bursæ recurred and although usually responding well to reinjection tended to recur constantly We no longer treat such bursæ with hydrocortisone

The painful tender indurated areas in muscle musculo tendinous regions, and tenoperiosteal junctions which often follow trauma showed a particularly successful response to hydrocortisone Results were often dramatic and considerably shortened the periods of physiotherapy otherwise often required

The results in the treatment of early Dupuytren s contracture are encouraging but sufficiently few cases have been tried to warrant conclusions

The over all recurrence rate in the present series is about 10% Most of the cases have been followed for six to nine months or longer which fact probably explains why this figure is rather higher than in any of the previously reported series and it may well be even higher after longer periods of time have elapsed.

Hydrocortisone by its anti inflammatory ' action which has not yet been explained appears to be of great value in treating acute non specific lesions of soft tissues its efficiency is greatest in the early acute cases where inflammation is presumably at its peak and least in cases of long standing in which the inflammation has probably subsided and fibrosis is prominent

The older the patient the less readily he responds to treatment

The apparent absence of toxic effects in the dosage used further enhances the value of hydrocortisone as a therapeutic agent

## Summary

200 cases of soft tissue lesions were treated by local injection of hydrocortisone

This treatment led to complete resolution of symptoms in 80% of the cases and was ineffective in 10%

A recurrence rate of 10% was observed during a nine month follow up Most recurrences started within three months.

The combination of 2% procaine and hyaluronidase with the hydrocortisone has proved a valuable adjunct

We are indebted to Dr K MacLean for supplies of hydro cortisone acetate and to Mr Charles Engel, of Guy s Hospital photographic department for the illustrations

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# LIGATION OF THE POPLITEAL VEIN FOR ULCERS OF THE LEG

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The results of ligation and excision of a segment of the popliteal vein for leg ulcers of venous origin in patients followed for an average of 4½ years are described here, together with an investigation into the state of the ligated veins by venography and measurement of the venous pressures

This inquiry was begun because the longest reported follow up of such cases is 2½ years (Bauer 1950), the results in the present series at 4½ years differed radically from those at 2 years, the late postoperative state of the ligated veins has not previously been investigated

## Method

The clinical results have been assessed solely on the state of the ulcers, and no account has been taken of subjective symptoms (e g , pain) and signs (e g , the amount of swelling of the feet and legs) which are difficult to assess

The venograms were ascending and done by the method of Moore (1949), which consists, in brief, of injecting diodone into any vein on the foot of the supine patient , using a tourniquet at the ankle to occlude the superficial veins and to force the diodone into the deep venous system , and applying a tourniquet to the thigh to occlude both the venous return and the diastolic inflow of arterial blood

The venous pressures were measured in any convenient vein in the foot by the method of Walker and Longland (1950)—i e , a ' Polythene ' tube is put into the vein and connected to a reservoir of heparinised saline solution and a manometer, and the venous pressure is taken to be that pressure at which the blood is just prevented from proceeding along the polythene tube The pressures taken were the standing pressure , the pressure when the patient was standing/walking lifting the feet about 18 inches 30–40 times a minute , and the pressure standing/walking with a tourniquet below the knee tight enough to occlude the superficial but not the deep veins

## Clinical Results

13 legs were examined The results at an average of 2 years after popliteal ligation (Moore 1953) were 8 healed, 1 healed but wearing an elastic-webbing bandage since operation, and 4 no change The results at an average of 4½ years are 2 healed, 1 healed but wearing an elastic-webbing bandage since operation, and 10 ulcerated Hence of the 13 legs 4 showed no improvement at time , 6 healed for periods of 9 months to 5 years then broke down , 1 is healed but has worn bandages since operation and may therefore be cure that or by the operation , and only 2 can be consid an unqualified success

### Venographic Findings

11 legs were examined at an average of 3½ y postoperatively. The findings were the same in namely, that the gap in the popliteal vein had bridged by a dense plexus of large channels (see fig

### Venous Pressure

The same 11 legs were examined at an average of years postoperatively, and the readings were comp with the readings in the opposite leg when only 1 pop vein had been excised The findings are set out in accompanying table, which shows that the avera in the venous pressure with standing/walking standing/walking with a tourniquet below knee about 22 mm Hg in each case, whereas it has been that the usual fall in pressure where the deep ve normal is about 44 mm Hg (Moore 1954)

The table also shows that, with 1 exception, the great difference between the falls of pressure on th with an intact popliteal vein and that on the si which the vein has been ligated

## Discussion

The principle of popliteal ligation is based on assumptions (1) that the gravitational syndrome re from a column of blood, in the deep veins, extending the heart to the feet unsupported by adequate v valves, these being either congenitally absent or dest by previous phlebitis or incompetent through dila of the deep veins , and (2) more important still, th absence of valves prevents the normal fall in v pressures with exercise It was therefore thought the unsupported column should be broken by ligat the popliteal vein (Bauer 1948)

That the column can be interrupted is evident, that new large venous channels would form to tak place of the popliteal vein seemed likely—and th fact happens All the legs examined showed these co collaterals (see figure) , the collaterals being so big it is impossible to believe that the column of blood in legs is in any way interrupted at the site of operatio

*As regards the venous pressures* with exercise it is to see how ligation of the popliteal vein would h indeed, the obstruction of the main venous channe operation should cause a rise of pressure distally, exercise, at least in the immediate postoperative per

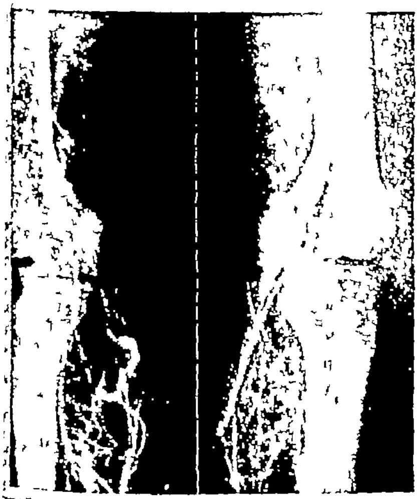
VENOUS PRESSURES IN 11 LEGS 3½ YEARS AFTER LIGATION OF THE POPLITEAL VEIN

| Case no | History of old deep phlebitis | Operation done | Result of venogram on side of pop lig | Pressure (mm Hg) |  |  |  | Falls in pressure (mm Hg) |  |
|---|---|---|---|---|---|---|---|---|---|
|  |  |  |  | Standing |  | Standing/ walking | Standing/ walking with tourniquet | Standing/ walking | Standi walki with tourni |
| 1 | Doubtful | Rt nil lt pop lig | Large collaterals round gap | Rt | 90 | 80 | 71 | 10 | 19 |
|  |  |  |  | Lt | 90 | 64 | 62 | 26 | 28 |
| 2 | Yes | Rt nil lt pop lig , lt Trendelenburg |  | Rt | 90 | 50 | 32 | 40 | 58 |
|  |  |  |  | Lt | 90 | 80 | 80 | 10 | 10 |
| 3 | Yes | Bilat pop lig | , | Rt | 88 | 58 | Not done | 30 |  |
|  |  |  |  | Lt | 88 | 52 | 52 | 36 | 36 |
| 4 | Yes | Bilat pop lig , bilat Trendelenburg | , | Rt. | 89 | 78 | 76 | 11 | 13 |
|  |  |  |  | Lt | 90 | 70 | 70 | 20 | 20 |
| 5 | Yes | Rt Trendelenburg lt pop lig |  | Rt. | 88 | 60 | 45 | 28 | 43 |
|  |  |  |  | Lt. | 88 | 60 | 60 | 28 | 28 |
| 6 | Yes | Bilat pop lig , bilat Trendelenburg | } | Rt | 92 | 60 | 66 | 32 | 26 |
|  |  |  |  | Lt | 90 | 65 | 64 | 35 | 36 |
| 7 | No | Rt pop lig , lt nil |  | Rt | 90 | 80 | 74 | 10 | 16 |
|  |  |  |  | Lt | 90 | 30 | 48 | 60 | 42 |
| 8 | Yes | Rt nil lt pop lig lt Trendelenburg | , | Rt | 98 | 59 | 60 | 39 | 38 |
|  |  |  |  | Lt | 100 | 100 | 100 | 0 | 0 |
|  |  |  |  | Average falls in ven press on side of pop lig |  |  |  | 21 5 | 41 |
|  |  |  |  | Average fall on side with intact pop vein |  |  |  | 35 | 40 |

d this had been shown to happen (De Camp et al 1951 yd et al 1953) The present cases show similar ults 3½ years after operation there being an average l of pressure on standing/walking and standing/walking h tourniquet below the knee which is much less than the normal and much less than in the unoperated leg the same patient

## Conclusions

t therefore seems that the basis of the operation is ound and the long term results although judged very few cases, are shown to be poor Nevertheless s of interest to speculate why any of these cases do ll (3 of these which had proved most intractable to the al measures remained well for 5 years after the ration and 2 continue to do so)



nding venograms 4 years after 1½ inches of right popliteal vein had been excised : A operated leg ; B unoperated leg

ote copious large collaterals which have taken place of ised segment and excellent filling of femoral vein through e collaterals. Venous pressures (mm Hg) measured at e time were as follows :

| | *Standing* | *Standing/walking* | *Standing/walking with tourniquet* |
|---|---|---|---|
| leg | 90 | 80 | 74 |
| leg | 90 | 30 | 48 |

## Summary

The clinical results are given of the ligation of 13 pliteal veins for ulcers of the leg, at an average of 4½ ars postoperatively

The veins of the leg after popliteal ligation were amined in 11 cases by ascending venography and by asurement of the venous pressures

The clinical results were bad and venography and venous pressures showed that the theory of the operation has an unsound basis

Nevertheless 3 intractable ulcers remained healed for 5 ears after the operation—no explanation is given for his—and 2 remain healed

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# STILBŒSTROL PHOSPHATE AND PROSTATIC CARCINOMA

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ANTIANDROGENIC measures such as castration and œstrogen therapy have been widely used in the treatment of carcinoma of the prostate However there has been much discussion about the mechanism of action of œstrogen on the prostatic epithelium Thus Szego and Roberts (1953) claim that œstrogens have to be activated by the liver before they can have any effect and Chamorro (1950) believed that they act indirectly by restricting the production of androgenic hormones. However Lasnitzki (1954) has shown in tissue-culture of mouse prostate that œstrogens act directly on the prostatic epithelium

Several workers have advocated the use of œstrogen phosphates in the treatment of prostatic carcinoma on the assumption that such phosphates would be dephosphorylated in the prostate by its phosphatases and thus presumably more effectively localised in the prostate It therefore seemed important to see whether one of these œstrogen phosphates—namely, diethylstilbœstrol diphosphate—could be dephosphorylated in vitro by the phosphatases of the prostate

Fresh human prostatic tissue and fresh prostate liver spleen brain and kidney of rats were separately homogenised in an Elvehjehm Potter glass homogeniser To show activity in an acid medium 0 5 ml of acetate buffer pH 5·0 containing 10 mg of the œstrogen phosphate was added to 0·3 ml of different concentrations of the homogenate : 1 : 10 1 : 20 ; 1 : 40 and 1 80 To show activity in an alkaline medium barbitone-hydrochloride buffer pH 8 0 was used The mixture was incubated for one hour at 37 C and the phosphatase activity was measured by estimating the amount of phosphorus liberated from the substrate by the method of Allen (1940) Suitable controls were made by incubating the same substrate-buffer mixture without homogenate and by using an inactivated homogenate

Human prostate phosphatases both acid and alkaline proved highly effective in hydrolysing the stilbœstrol phosphate. Similar results were obtained with rat tissues which are known to contain large amounts of acid and alkaline phosphatase Attempts to show the reaction histochemically in an acid medium failed because lead ions precipitated the substrate

This ability of prostatic tissue to hydrolyse stilbœstrol phosphate might justify the claim of Druckrey and Raabe (1952) and Wilmanns (1954) that stilbœstrol phosphate has an organ specific chemotherapeutic effect in the treatment of prostatic carcinoma. We found however, that this substance was dephosphorylated by rat tissues other than the prostate On the other hand, a carcinomatous prostate produces far more acid phosphatase than any other organ and might therefore be expected to hydrolyse much more stilbœstrol phosphate

It remains to be seen whether the ability of the prostate to hydrolyse stilbœstrol phosphate is due to its specific acid phosphatase or to a specific phos Bourne (1954) has shown histochemically differences in the localisation of the reaction rat tissues when stilbœstrol phosphate substrate compared with the results obtai phosphate or with œstrone phosphate that there are one or more specific œs

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* In receipt of a grant from the Brit

A further problem under investigation in this laboratory is the possibility of increasing the therapeutic value of œstrogen phosphates in treating prostatic carcinoma by incorporating $^{32}P$ in the molecule It may be possible in this way to use two therapeutic agents—the stilbœstrol molecule and radioactive phosphorus—to attack the malignant prostatic cells

We are indebted to Dr A. L Morrison, director of research, Roche Products Ltd , and Asta Werke, A G , for supplies of diethylstilbœstrol diphosphate

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# DISSECTING ANEURYSM OF THE AORTA

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THE following cases are reported to show that patients may survive external rupture of a dissecting aneurysm of the aorta After a remission lasting four days case 1 died suddenly from a recurrence of bleeding, but case 2 survived for a year and returned to his ordinary work before he died of cerebral hæmorrhage Necropsy in case 2 revealed a healed dissecting aneurysm with no trace of either previous hæmorrhage or external tear of the aorta

## Case-reports

**Case 1** —An obese intelligent man, aged 60, was admitted to hospital on Dec 27, 1950, with three years' history of precordial pain and dyspnœa on exertion Twelve days before admission, while straining at stool, sudden intense pain between the shoulder blades caused him to roll about the floor, screaming in agony The pain was eased by morphine and disappeared after ten hours The patient remained in bed and had no further trouble until the day before admission, when, while sitting on a bedpan straining at stool, he experienced a sudden sensation of a vice-like grip on his neck He could not move his neck, which rapidly became extremely swollen, and he developed urgent dyspnœa Thinking he was about to die, he called for his wife and clasped her tightly to his chest until he experienced partial relief of symptoms a few minutes later

*On admission* he had conspicuous swelling and bruising of his neck On the right side of his chest was a leaf shaped bruise which was a facsimile of the cut out pattern of the dress his wife was wearing at the time of the embrace The pharynx was ensheathed in blood in the submucous layers The pulse was regular, rate 100 , the heart was enlarged to the left on percussion, and the heart sounds were normal, with no murmurs The blood pressure was 180/120 mm Hg in both arms The femoral pulses were present and equal No abnormality was found on examination of the abdomen, the lungs, and the central nervous system A blood count showed red cells 4,550 000 per c.mm white cells 10,500 per c mm (neutrophils 86%) , Hb 92% Electrocardiography showed evidence of ischæmia of the anterolateral surface of the heart but no evidence of myocardial infarction Radiographs of the chest and neck showed a prominent unfolded aorta , gross enlargement of the upper mediastinal shadow to the right , a very considerable increase in the prevertebral soft tissue shadow in the cervical and upper dorsal regions displacing the trachea and larynx forwards , compression of the trachea at root of neck , and gross compression of the supraglottic portion of the laryngopharynx These findings are consistent with a large hæmorrhage into the s[illegible]es The blood urea level was 36 mg per 100 ml

*Outcome* —The patient's condition was satisfactory until Dec 30, 1950, three days after admission, when he suddenly cried out with pain in his neck and died in a few minutes

*Necropsy Findings* —At the junction of the left subclavian artery with the aorta there was a split about a quarter of an inch long through all the coats of the aorta Behind this there was a massive collection of blood clot, extending upwards into the neck as far as the base of the skull, in the loose fascia between the cervical and thoracic vertebræ and the œsophagus The blood had infiltrated all the fa planes of the neck, the skin of the neck and right upper ch and the submucous tissues of the pharynx and larynx including the aryepiglottic fold From the site of rupture dissection between the adventitia and the media of the ao extended as far as the origin of the cœliac axis The ascend aorta was unusually free from atheroma The heart show moderate left ventricular hypertrophy and fairly extens coronary atheroma No further abnormalities were dem trable

*Comment* —Taken in conjunction with the history angina, the sudden onset of chest pain at first suggest myocardial infarction The later development of sudd swelling of the neck indicated hæmorrhage from a lar artery, and it became clear that the patient had sustain a dissecting aneurysm of the aorta which had ruptu externally It seems certain that the hæmorrhage, such force as to delineate the leaf pattern of his wi dress during an embrace, ceased within a few minut The patient's convalescence appeared to be satisfact until his sudden death four days later

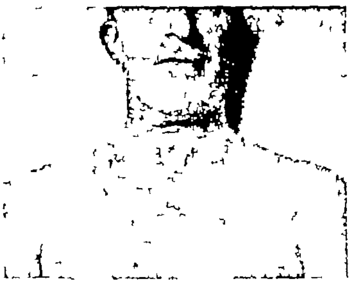
**Case 2** —A well nourished man aged 50, was admitted hospital on Jan 31, 1951 He had been well until 8 A.M t days previously Then, while walking about at home gradually developed dull aching pains over both scap Within two to three hours the pain moved to the epigastri and became very severe The patient retired to bed, and l in the day the pain became stabbing, each stab coincid with a beat of the heart The pain persisted in diminish intensity until 10 A M on the day of admission, when w lying in bed he suddenly cried out with intense pain betw the shoulders and immediately noticed a swelling of his n and a sense of suffocation Within a few minutes the n was much swollen and the patient became extremely anxio The pain was much easier when he reached hospital an ho later

*On admission* there was a conspicuous diffuse, soft, rather tender swelling of the neck The circumference of neck was $17^1/_2$ inches (he normally wore a 15 inch col His pulse rate was 85, pulse regular The cardiac apex 4 inches out in the fifth interspace The heart sounds w normal, and there were no murmurs The blood pressure 195/110 mm Hg in the right arm and 190/110 mm Hg in left arm The systolic blood pressures were 230 and mm Hg in the right and left legs respectively No abnormal was found on examination of chest, abdomen, or centr nervous system A ruptured dissecting aneurysm of the aor was provisionally diagnosed, and the patient was kept strictly at rest in bed

*Two days later* a massive bruise appeared over the upp chest and the neck (see figure) A blood count showed re cells 4,800,000 per c.mm , white cells 11,400 per c.mm (neutrophils 70%) , Hb 88% The erythrocyte sedimentation rate was 23 mm in the first hour (Westergren) Electrocardiography did not show evidence of myocardial infarction The Wassermann reaction of the blood was negative Radiography on Feb 5, 1951, showed an enlarged aortic arch.

*During the next few weeks* the patient had attacks of central chest pain, each lasting several hours, at about daily intervals The attacks were sudden and severe and usually required 'Omnopon' for their relief Radioscopy on March 27, 1951, showed that the posterior part of the aortic arch was extremely wide, the left border of the descending aorta (or aneurysm) extending well to the left and showing a small local bulge half way along its length , pulsation, not very pronounced, was seen in this descending portion The attacks of pain gradually diminished in frequency and intensity, and the patient was entirely free from symptoms at the time of his discharge on April 3, 1951

*After discharge* he attended as an outpatient at regular intervals At first he remained symptom free apart from occasional mild precordial discomfort He returned to work



2: widespread ecchymosis over neck and upper part of chest.

the end of July 1951 Examination on Sept 10 1951 wed that the blood pressure had risen to 280/100 mm Hg the right arm and 300/170 mm Hg in the left arm On r 14 1951 the patient reported that he got dyspnœa on king a few hundred yards His fundi now showed illœdema.

*admission*—On Jan 28 1952 the patient was admitted hospital in deep coma. While sitting at a desk he had had dden queer feeling and lapsed into coma within a few utes On admission an hour later he was deeply uncon us, with *stertorous breathing pulse rate* [illegible] *and blood* sure 220/120 mm. Hg His fundi showed bilateral illœdema and flame-shaped hæmorrhages He died a few rs later

*ecropsy* showed a dissecting aneurysm of the aorta nding from the end of the aortic arch for 8 cm Re-entry taken place, and a new endothelialised track was present re was no evidence of previous external rupture of the urysm or of hæmorrhage The left ventricle of the heart hypertrophied with patchy fibrosis of the myocardium coronary arteries showed severe atheroma but were ent The brain contained a massive hæmorrhage in the n, which extended up into the right basal ganglia and isphere

*Comment*—In view of the remarkable similarity to e 1 it seemed certain that this patient also had a ecting aneurysm of the aorta with external rupture, the pulsating nature of the pain supported that view lgore 1940) At necropsy a year later there was no lence of previous external rupture of the aneurysm the explosive nature of the hæmorrhage and its urrence two days after the onset of severe pain left le doubt that the aneurysm had so ruptured The urysm remained healed despite the later develop nt of malignant hypertension

## Discussion

External rupture is the commonest cause of rapid ath in cases of dissecting aneurysm of the aorta (David al 1947) *and few patients survive this complication* more than a few hours The present cases were usual not only because they survived sudden severe æmorrhages for four days and a year respectively but so because the hæmorrhage took place into the tissues the neck with dramatic swelling and with the later velopment of ecchymoses The physical findings ter rupture and hæmorrhage from a dissecting aneurysm e rarely so obvious as in the present cases, and recovery om this complication may be more common than is nerally recognised Necropsy at a later date as in e 2, may not show evidence of previous hæmorrhage of external rupture of the aorta

The fact that hæmorrhage from a dissecting aneurysm the aorta is not invariably and immediately fatal is portant because cases of this kind may readily be nfused with myocardial infarction and treatment with ticoagulants may be instituted with disastrous results rumfitt and Rankin (1954) report an example of this therapeutic error The difficulty in diagnosis between dissecting aneurysm and myocardial infarction was first discussed by White et al (1934) The difficulty persists for in 58 cases of dissecting aneurysm reported by Levinson et al. (1950) the mistaken diagnosis of infarction had been made in 20 (34 5%) The electrocardiograph is usually abnormal in cases of dissecting aneurysm of the aorta but only rarely does it show evidence of myocardial infarction (David et al. 1947) However in endeavouring to start anticoagulant therapy as soon as possible in cases of presumed myocardial infarction, such treatment may be given in anticipation of electrocardiographic confirmation If such treatment is mistakenly given in cases of dissecting aneurysm particularly with external rupture it will probably prejudice the small chance of the patient s recovery

## Summary

2 cases of survival after external rupture of a dissecting aneurysm of the aorta are recorded In case 1 the survival was for four days and at necropsy the site of the hæmorrhage was clearly demonstrable Case 2 lived for a year and after death from cerebral hæmorrhage no trace of the external rupture could be found though the clinical course left no doubt of its occurrence

The necropsies were done by Dr M G Fitzgerald (case 1) and Dr J G Jackson (case 2)

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# A *CASE OF SARCOIDOSIS AND THREE* CASES OF ATYPICAL TUBERCULOSIS IN A FAMILY

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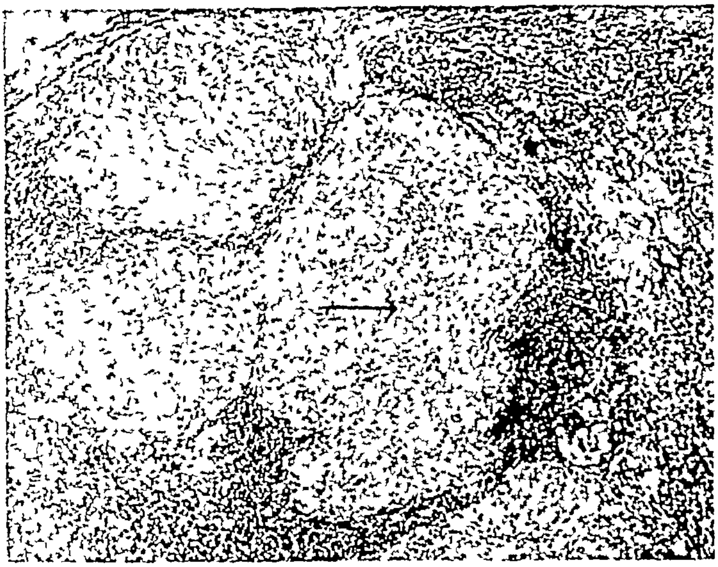
IN view of the conflicting views on sarcoidosis as regards both ætiology and definition the following report of one case of sarcoidosis and three cases of an apparently related condition in a family is of interest

Sarcoidosis as now defined (Scadding 1950 Cowdell 1954) is that condition or group of conditions in which is found throughout the affected tissues a definite histological pattern which is described by Scadding thus

> Epithelioid tubercles, as a rule clearly defined within the affected tissues with only slight round cell infiltration in their vicinity without any central caseation with or without Langhans type Giant cells and with or without the peculiar inclusion bodies within these cells described by Schaumann (1941)

This definition has great advantages over previous ones in that it is rigid and contains few 'permissive phrases. There should be no doubt once the affected tissue has been examined histologically about whether the case comes within the definition or not Such a rigid definition however carries with it certain disadvantages occasional cases somewhat resemble sarcoidosis both clinically and histologically but do not quite fit the definition Three of the present cases fall into this category The lesions in each showed minimal central caseation which excludes sarcoidosis Such cases are difficult to classify We have reluctantly called them 'atypical tuberculosis,' realising that this is not a satisfactory name because it appears to assume that tuberculosis is the cause of the condition



Biopsy specimen of axillary lymph-gland from case 1, showing area of minimal central caseation (arrow)

The family consists of the parents, five sons, and two daughters The youngest child is now aged 17 The elder sister and two of the brothers have refused examination The mother and the father have shown no abnormality

**Case 1** —The eldest son, aged 27, was found to have bilateral scattered pulmonary shadows on mass radiography in June, 1952, and was admitted to a sanatorium No tubercle bacilli were found in his sputum, and he was negative to 100 tuberculin units in a Mantoux test He developed signs of peripheral neuritis, became semicomatose, and was transferred to a general hospital For weeks he continued to have low grade pyrexia and remained very ill

*Investigations* —Lumbar puncture produced cerebrospinal fluid (C S F ) containing no cells, protein 240 mg per 100 ml , and an increased amount of globulin A Wassermann reaction was negative Liver biopsy, bronchoscopy, a blood count, erythrocyte sedimentation rate (E S.R ) plasma protein levels, and radiographs of hands and skull were all normal Vaccinated with B C G the patient did not subsequently react to Mantoux 100 tuberculin units In December, 1952, a biopsy specimen of a right axillary lymph gland contained nodular granulomatous lesions, many of them undergoing fibrosis There were also numerous lobulated scars which represented the final stage of healing of granulomata The granulomatous lesions were composed of epithelioid cells, and some showed a suspicion of central caseation Most of the lesions would be classified as sarcoidosis, but some were fairly typical tubercles (see figure) Tubercle bacilli were not found on Ziehl Neelsen staining

*Treatment and Progress* —In view of this report the patient underwent anti tuberculosis chemotherapy without obvious improvement His chest radiographs remain unchanged, but his neurological lesion has gradually improved, and two years after first presenting he was well enough to return to light sedentary work Repeated sputum cultures during this time have all proved negative for tubercle bacilli

**Case 2** —Case 1's younger sister, aged 22, was radiographed in 1952 as a contact of case 1 and found to be normal then and again in February, 1953, when she was negative to 10 tuberculin units in a Mantoux test In August 1953 she was found to have gross enlargement of her hilar lymph glands and was admitted to hospital, without symptoms or signs

*Investigations* —Another Mantoux test with 100 tuberculin units was negative, and sputum cultures did not grow any tubercle bacilli Plasma protein levels a blood count, and radiographs of the hands were all normal A biopsy specimen of liver contained several small well defined nodules of epithelioid cells surrounded by a narrow zone of lymphocytes No giant cells were seen The histological appearances were those [illegible] idosis

*Treatment and Progress* —The patient receiv a three month course of anti tuberculosis chemo therapy, and radiographs subsequently show considerable improvement She remains well

**Case 3** —A brother of cases 1 and 2, a 24, attended hospital with enlarged submenta lymph glands in May 1953 In March, 1954, h was seen at the chest clinic with a year's histor of cervical swellings which were gradually becom larger

*Investigations* —He was positive to 100 tuber culin units in a Mantoux test A blood-co E S R , radiographs of chest and hands, pl protein levels, alkaline phosphatase, and se calcium levels were all normal In May, 1954 biopsy specimen of a submental lymph-gl showed that the structure of the gland had be largely superseded by well demarcated gran matous masses consisting mainly of epitheli cells Some of the masses showed early cent caseation, but no giant cells were seen, acid fast bacilli were found by Ziehl Ne staining

*Treatment and Progress* —The patient was trea with streptomycin and *p* aminosalicylic acid July–October, 1954 Some of the enlarged gl definitely regressed, but a further gland bec palpable in the left occipital region

**Case 4** —Another brother, aged 22, noticed a swelling beneath the angle of his jaw in 19 this was also noted on his discharge from the Army in 1 When he was radiographed as a contact in 1953, the c radiograph showed increased hilar shadows, but these passed as normal at the time He first attended the chest c in March, 1954, when many enlarged lymph glands were fo on both sides of his neck and in both inguinal reg and radiography of his chest showed much enlarged h shadows

*Investigations* —He was negative to 100 tuberculin unit a Mantoux test A blood count, E S.R. plasma protein le alkaline phosphatase, serum calcium level, and radiogr of hands were all normal In May, 1954, a biopsy spec of submental lymph gland showed that the fatty t contained the remains of small lymph nodes which had be almost completely superseded by fairly well defined collecti of epithelioid cells, some of which showed slight cent caseation No giant cells were seen The pathological le was the same as that seen in the glands of case 1 Acid f bacilli were not found

*Treatment and Progress* —The patient was treated *p*-aminosalicylic acid in July–October, 1954 The enla glands gradually decreased, but he developed further palp glands in his axillæ

## Other Recorded Families

Though there is a wealth of literature on the subj of sarcoidosis, there are but few references to it siblings, and in most of the published cases of sarcoido in siblings the evidence is only clinical and not histolog

The first published cases of sarcoidosis in siblings w those of Sellei and Berger (1926), who described a family seven siblings, of whom five had histologically proved cutaneo sarcoidosis

Robinson and Hahn (1947) described two Negro famili who had sarcoidosis In one family two of three sibli had sarcoidosis involving lungs, skin, and uveoparotid regio and in one of them the sarcoidosis was histologically proved In the other family three of five siblings had histologicall proved sarcoid One of these was found at necropsy to have lesions of sarcoid in lungs, kidneys, and other organs, and definite tuberculosis of axillary lymph glands, but it doubtful if this case could be accepted as a case of sarcoido under the present definition Another member of this fami later developed pulmonary tuberculosis with tubercle bac in the sputum All these cases were tuberculin negative to a dose of 10 T U

Bickerstaff (1940) described two brothers who were und observation for years and whose condition followed the benig course with eventual resolution more often associated with sarcoidosis Both these patients had a lymphadenopath and lung lesions and were tuberculin negative to a dose o

0 T U and both cases were histologically proved by gland iopsy

Dressler (1938, 1939) described two families in which two blings were affected with clinical sarcoidosis but there was o histological confirmation.

MacCormac (1939) described two sisters with cutaneous arcoidosis, one of the two cases being proved histologically

Boggild (1944) described two members of a family with teitis tuberculosa cystica, and one of these also had mphadenopathy but no histological confirmation was ven.

Jacobsen (1936) described two sisters aged 8 years and 1 years, who had a generalised lymphadenopathy including ediastinal glands One of these girls had osteitis tubercu sa cystica, and one of them was strongly positive to 10 T U berculin, whereas the other sister was negative even to as gh a dose as 1000 T U Excised epitrochlear glands in each se gave a histological picture which was neither that of rcoidosis nor that of tuberculosis with caseation Portions those glands were injected into a guineapig and into a bbit with negative results The later history of the two ses is interesting because one of the girls died of tuberculous ritonitis and the other of tuberculous meningitis Their ther died of pulmonary tuberculosis Histological pictures Jacobsen's article are almost identical with those seen in e present cases 1 3 and 4

## Discussion

Three of our cases do not come within the modern finition of sarcoidosis We have called them atypical berculosis following the precedent of Cameron (1950) nd Jacobsen (1936) and implying that they resemble berculosis histologically without being absolutely pical, and that they do not fulfil the criteria of sar idosis They might equally be called atypical rcoidosis, but we feel that this would be wrong cause it would tend to widen the definition of sar idosis and would lead back to the chaos in terminology at Scadding (1950) has done so much to clear

Whatever *may be the cause of the lesions in the* others, it seems reasonable to assume that the sar idosis in their sister might have a similar cause If a berculous ætiology for the present cases of sarcoidosis accepted, the lesions in the brothers may represent ansitional types between one form of sarcoidosis and berculosis However, the only evidence in these cases at there may be a tuberculous ætiology lies in the cts that (1) histologically some of the lesions resemble berculosis and (2) four cases in a family may indicate n infective cause. There is really no other evidence a tuberculous ætiology A positive tuberculin test one brother does not necessarily indicate tuberculosis the cause of his glandular lesions nor do negative ts in the others exclude tuberculosis (Hoyle 1947)

Response to anti tuberculosis chemotherapy is also nreliable evidence in the present cases The one that ppeared to benefit most from the treatment was the se of sarcoidosis One of the others showed no response t all The other two showed some decrease in their iginal glandular swellings but developed new lesions hile undergoing chemotherapy All these changes might well have occurred without any therapeutic interference

Other known causes of sarcoidosis, such as beryllium and chronic brucellosis do not appear to be relevant to this family

A further *difficulty in such cases is that a histological* diagnosis must rest on the amount of affected tissue examined microscopically Perhaps if the biopsy pecimen of liver in the girl had been larger or if an affected gland had been available for biopsy they might have shown lesions like those seen in the brothers—i e with minimal central caseation A similar argument might be applied *to many cases of sarcoidosis*. Such speculation is, of course taking the matter beyond the available data, but it does make one realise that there are imperfections in a rigid histological definition The whole matter of sarcoidosis is likely to remain imperfect until the conditions that at present are included under *this heading can be classified according to cause and* pathogenesis

So far as our present state of knowledge goes, it seems to us that the most plausible explanation of these cases is that tuberculosis under certain conditions is the cause of one type of sarcoidosis, and that the lesions in the brothers might be transitional between sarcoidosis and tuberculosis

## Summary

In seven siblings, of whom only four were examined there were three cases resembling sarcoidosis and one case of histologically proved sarcoidosis

Three of the cases were negative to 100 tuberculin units in a Mantoux test and in none of the four were either giant cells or tubercle bacilli found

The case that appeared to benefit most from anti tuberculosis chemotherapy was that of sarcoidosis

It seems reasonable to suggest that the occurrence of four somewhat similar cases in siblings was due to infection by the same ætiological agent

*If tuberculosis was responsible, the lesions in the* brothers might be transitional between sarcoidosis and tuberculosis

We wish to thank Dr C J Stewart and Dr Ronald Jones for permission to publish these cases and for the help and advice that they have given Dr A B Lintott for the histological reports and advice and Mr S W Patman, of *the department of pathology of the University of Cambridge* for the photomicrograph

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# FATAL AIR-EMBOLISM ASSOCIATED WITH RUPTURED UTERUS

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Air embolism as a complication of obstetric practice was first mentioned by Ligallois (1828) and the three earliest published cases in this country were reported by May (1857) Since then isolated cases have been described the most recent by Waldrop (1953) who collected 17 previously published cases and added 1 of his own of fatal air embolism during labour or in the puerperium he did not include cases in early pregnancy and associated with tubal insufflation or with attempts to procure abortion

Gough (1924) emphasised the number of fatalities due to air-embolism accompanying the treatment of placenta prævia by bipolar version and in modern practice there appears to be a significant association with cæsarean section, fatal cases having been recorded by Osborn and Dawson (1938) Marshall (1939) and Cody and Windrow (1951) A H C Walker has personally communicated to us details of an unpublished case

Although many of the early published cases were probably the result of infection with gas-forming anaerobes, fatal air embolism in obstetrics is evidently not exceptionally rare Figures supplied by the Registrar-General show that in the five year period 1948–52 in England and Wales 7 deaths were notified as "air embolism complicating labour "

We believe that the association of silent rupture of the uterus and air embolism, which occurred in the two cases described here has not hitherto been recorded

## Case-reports

**Case 1** —A married primigravida, aged 32, with no significant medical or surgical history, had a normal antenatal period except for slight pre eclamptic toxæmia, which developed at thirty eight weeks' gestation

*Labour* began spontaneously a week before term The presentation was cephalic, the vertex being deeply engaged in the pelvis, and the outlet was not contracted The first stage of labour was normal and lasted twenty two hours Fifty minutes after full dilatation the presenting part was visible and advancing steadily, but the maternal pulse rate, which had been 80, suddenly increased to 140 No cause for this was then apparent, but in view of this evidence of maternal distress the labour was terminated with the aid of forceps under general anæsthesia No difficulty was experienced in the extraction The blades were correctly applied, no rotation was needed, and traction was minimal Intravenous ergometrine 0 5 mg was given after delivery of the anterior shoulder, and the separated placenta was immediately expressed Another dose of ergometrine was given five minutes after delivery because the uterus was relaxing and there was slight hæmorrhage from the vagina

*Immediately after delivery* the pulse rate had increased to 170 and the blood pressure was 90/60 mm. Hg Thirty minutes later the pulse rate had increased to 176 and the systolic blood pressure had fallen to 50 mm Hg The patient had slight air hunger and pallor but no cyanosis Her uterus still tended to relax, but hæmorrhage was slight in proportion to the degree of collapse An infusion of 'Dextraven' was started, which was followed by transitory improvement

*Two hours after delivery* recovery from anæsthesia was complete, but the patient was apprehensive and complained of severe backache Her uterus was well contracted, and she had no abdominal tenderness Her systolic blood pressure had risen to 60 mm. Hg At this stage her general condition again deteriorated, and whole blood was substituted for the dextraven Despite this blood transfusion, given rapidly but without positive pressure, the deterioration was pro progressive, air hunger became more severe, and death took place two and a half hours after delivery The total amount of blood lost was estimated at less than 500 ml

At *necropsy*, six hours after death, the right auricle and ventricle were collapsed, and the pulmonary artery contained large bubbles of gas The posterior wall of the lower segment of the uterus was excessively thin and hæmorrhagic, with a complete transverse laceration 1 inch long at the level of the internal os There was only scanty bloodstained fluid in the peritoneal cavity Histological examination of the pulmonary vessels showed no evidence of amniotic fluid Death was considered to be due to air embolism following rupture of the uterus, the route of entry of the air being either the edge of the laceration or the normally situated placental site

**Case 2** —A married woman, aged 40, with no significant medical or surgical history, was in her seventh pregnancy She gave a history of six normal full time deliveries, of which the most recent had been followed by a postpartum hæmorrhage and subsequent curettage Her largest baby was said to have weighed 12 lb at birth

*Labour* came on prematurely, after a normal antenatal period, at thirty four weeks gestation, when she was admitted to hospital The presentation was cephalic, with the vertex engaged in the pelvic brim Labour progressed normally, and a live baby weighing 5 lb 5 oz was born after a first stage lasting five hours and a second stage lasting ten minutes The placenta was expressed five minutes later, after normal separation A brisk hæmorrhage took place before, during, and after the delivery of the placenta amounting to 500 ml Intravenous ergometrine 0 5 mg produced a satisfactory response The patient's general condition was good, with no apparent ill effects from the hæmorrhage

*Ten minutes later* the patient suddenly had nausea and air hunger and became restless, apprehensive and much cyanosed Her uterus was well contracted, and she had no external bleeding Her pulse rate was 110 and systolic blood pressure 60 mm Hg The degree of shock was considered to be out of all proportion to the amount of blood lost A dextran infusion was started pending the cross matching of whole blood Twenty minutes later the patient was worse, complaining of thirst, lower abdominal pain, and intense backache She was deeply cyanosed, and her air hunger had increased, but her consciousness was not impaired at [illegible] time Shortly afterwards she vomited, had a convulsion and died

At *necropsy*, fourteen hours after death, when the right ventricle was opened gas escaped and the right side of the heart contained a little frothy blood The superior [illegible] inferior venæ cavæ were distended by air, as was the right ovarian vein Compression of the lungs expressed air from the pulmonary vessels A vertical laceration on the left side of the uterus, extending into the broad ligament, was 1½ inches long and situated about 1 inch above the internal os. The placenta was normally situated The pelvic tissues on both sides were emphysematous, and an area of hæmorrhage and emphysema extended upwards on the left side behind the colon as far as the diaphragm There was no blood in the peritoneal cavity Histological examination of the lungs showed no evidence of amniotic fluid Death was considered to be due to air embolism following incomplete rupture of the uterus, the route of entry of the air being uncertain

## Discussion

In cases 1 and 2 the true cause of death was [illegible] suspected before necropsy, although the silent rupture of the uterus was considered in each case In case [illegible] in which there was no interference during labour, the rupture could only be spontaneous In case 1 the possibility that the injury was caused through trauma by the obstetric forceps cannot be excluded, although this is thought to be unlikely because of both the sequence of events and the situation of the tear It is assumed that the sudden rise in the maternal pulse rate directly followed spontaneous rupture, which was otherwise silent

Fatal air embolism in labour or in the puerperium is generally assumed to follow entry of air into the venous circulation through the placental site Possibly the route of entry in cases 1 and 2, as in cases associated with cæsarean section, was through the venous sinuses in the region of the damaged uterine wall Whether manipulation of the uterus during expression of the placenta could be a factor or not is uncertain

Although both cases 1 and 2 received intravenous fluid in their terminal stages, we consider that this route of entry of air can be acquitted because the symptoms and signs of air embolism had made their appearance before the intravenous infusions were set up

Probably the fatal outcome may be explained by the fact that under certain conditions the pregnant uterus is peculiarly adapted to becoming the site of air entry into the circulatory system Entrance is usually through one or more open vessels subjacent to the separated or partly separated placenta Alternatively a portal of entry may be created either by surgical division of vessels, as in cæsarean section, or by the opening up of vessels produced by the laceration of the uterine wall concomitant with various degrees of uterine and cervical rupture

Air embolism is a not uncommon complication of many diagnostic and therapeutic procedures using air under pressure, and can also occur when the air is not under pressure For this to happen there must be a break [illegible] the continuity of a blood-vessel, and the open vessel must contain blood at a lower pressure than the surrounding "atmosphere"

Cody and Windrow (1951) believe that the symptom f air-embolism are produced in two ways :

(1) The heart fills with compressible air with the result at, with each beat, much force is expended in compressin e air rather than in driving the blood onwards into the ssels.

(2) The blood is whipped up into a froth and reaches the ngs in such a state that it interferes with the normal ge ous change—that accounts for the air hunger and anoxia

The usual conception of air-embolism is a sudden vere chest pain followed almost instantaneously by ath That the terminal process may be much more adual is illustrated by the present cases and many her published ones. Osborn and Dawson (1938) phasise that in air-embolism followed by death after short interval the cardinal sign is pallor whereas if ath is delayed this is followed by cyanosis The other lient features they mention are sudden onset shock t hunger and restlessness To these we should add vere and intense backache which was noted in both of e present cases and in a further fatal case not associated ith uterine injury described to us personally by 8 Leverton.

In retrospect the most striking impression gained om the present cases was their close similarity to the -called obstetric shock occurring after labour and not sociated with severe hæmorrhage Although many ch cases are said to be due to prolonged labour pre isting anæmia &c such explanations are often satisfactory especially where the patients recover ithout any, or with only minimal treatment and sub quently show no evidence of anæmia or other abnor ality We suggest that some such cases may be plained by minor degrees of air-embolism insufficient produce rapid death, the air *in the cardiovascular* stem being finally absorbed Proof however of this position would be almost impossible.

No successful attempt has yet been made to treat tablished air-embolism by cardiac aspiration but lore and Duteil (1905) describe an unsuccessful effort a male patient We feel that in theory the condition eminently treatable and if a patient develops the ysical signs and symptoms and appears to be at the int of death the somewhat heroic step of cardiac piration may be justifiable

We suggest that *as a prophylactic measure* during pression of the separated placenta the patient's legs ould be maintained in abduction to secure patency of e introitus and so to prevent positive pressure of air the vagina if a second attempt at expression is neces ary Marshall (1939) appears to imply similar principles prophylaxis in cæsarean section

At necropsy it is important to bear in mind the ssibility of air-embolism in all fatal cases of so-called stetric shock

## Summary

2 fatal cases of air-embolism associated with ruptured terus are described

The probable mechanism and possible association with -called obstetric shock are discussed and prophylactic steps are suggested

We are indebted to Prof W I. C. Morris, Dr J W A Hunter and Miss Eleanor Mills for permission to publish, and to Dr F A. Langley and Dr J Davson for the necropsies.

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# HYDROTHORAX COMPLICATING ASCITES

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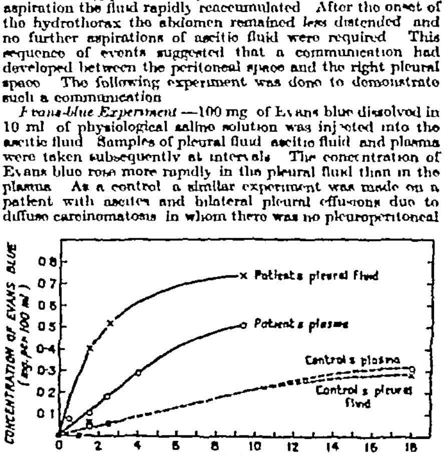
A SMALL collection of fluid in the pleural space is a common complication of ascites due to cirrhosis of the liver A large hydrothorax does not occur in more than 1% of cases (McKay et al 1947) A rare type of massive hydrothorax complicating ascites due to cirrhosis of the liver is characterised by a sudden onset and the fluid reaccumulates rapidly after repeated aspirations of very large volumes The appearance of the hydrothorax often coincides with a considerable diminution in the amount of ascites Single cases have been described by Martini (1892), James (1890) Preti (1920) Cassarini (1020), Maugeri (1929) Puech and Ratié (1933) Mauriac et al (1936) Goodman (1037), Christian (1937) Goffart (1938) Benedetti (1939) and Frothingham (1942) As in Meigs's syndrome the hydrothorax is usually on the right The following case is of interest because it was possible to show that the ascitic fluid had passed into the right pleural space through a small hole in the right hemidiaphragm

## Case-report

A barmaid aged 54 was admitted to hospital on Feb 8 1953 with gross ascites due to alcoholic cirrhosis of the liver Paracentesis abdominis was necessary on four occasions, and 34 pints of clear straw coloured ascitic fluid was removed it contained red cells 1200 per c.mm. leucocytes 2800 per c.mm (mainly lymphocytes) and protein 1 35 g per 100 ml. The patient was discharged on April 1 when her chest was clear Next day she suddenly became very breathless and was readmitted She now had a massive right hydrothorax and her abdomen was less distended 4 pints of clear straw coloured fluid was aspirated from the chest to relieve the dyspnœa ; it contained red cells 136 per c.mm leucocytes 60 per c.mm. (mainly lymphocytes) and protein 1 g per 100 ml The fluid rapidly re formed and in the next twenty days a further $12\frac{1}{2}$ pints was aspirated from the chest After each aspiration the fluid rapidly reaccumulated After the onset of the hydrothorax the abdomen remained less distended and no further aspirations of ascitic fluid were required This sequence of events suggested that a communication had developed between the peritoneal space and the right pleural space The following experiment was done to demonstrate such a communication

*Evans-blue Experiment* —100 mg of Evans blue dissolved in 10 ml of physiological saline solution was injected into the ascitic fluid Samples of pleural fluid ascitic fluid and plasma were taken subsequently at intervals The concentration of Evans blue rose more rapidly in the pleural fluid than in the plasma As a control a similar experiment was made on a patient with ascites and bilateral pleural effusions due to diffuse carcinomatosis in whom there was no pleuroperitoneal



Concentration of Evans-blue in pleural fluid and plasma of patient and of control.

communication. Almost the same concentrations of Evans blue appeared in the plasma and pleural fluid at the various times after the introduction of the dye into the ascitic fluid These results have been recorded graphically (see figure) It appeared certain that there was a direct communication between the peritoneal cavity and the right pleural space

*Subsequent Deterioration* —The patient's general condition steadily deteriorated in the next eight weeks Her chest was aspirated on several occasions, but the massive hydrothorax was still present when she died on July 24, 1953

*Necropsy Findings* —Before the body was opened, 100 mg of Evans blue in 10 ml of physiological saline solution was injected into the ascitic fluid The upper four ribs and part of the sternum were next removed In this way it was possible to inspect the upper surface of the undamaged diaphragm The right chest contained 3 litres of clear yellowish green fluid completely collapsing the right lung Heavily blue stained ascitic fluid was seen seeping through a very small hole (less than 1 mm in diameter) in the tendinous part of the right hemidiaphragm The hole was due to a localised separation of the tendinous fibres The edge of the hole was stained by the Evans blue Without this staining it would not have been seen There was another area of blue staining 5 cm anterior and medial to the first hole The stain had penetrated the diaphragm through another local separation of the tendinous fibres, but the overlying pleura was intact and there was no through and through communication No such lesions were found in the left hemidiaphragm The peritoneal cavity contained 1 litre of heavily blue stained fluid The liver showed severe cirrhosis There was no other significant abnormality

*Histology* —Serial sections of the diaphragm showed a small hole passing obliquely through the tendinous part There was no sign of inflammation

## Discussion

The occasional association of hydrothorax with ascites is well recognised Best known are those cases in which the ascites is due to an ovarian fibroma (Meigs 1954) Even when there are no pleural metastases, a malignant abdominal tumour can cause both ascites and hydrothorax (Gardiner and Lloyd Hart 1944, Deacon 1954) The point of great interest in these cases and in those of massive hydrothorax complicating ascites due to cirrhosis of the liver is the mechanism by which the hydrothorax develops Although other hypotheses have been advanced, it is now certain that in Meigs's syndrome the ascitic fluid somehow passes through the diaphragm and into the pleural space (Meigs 1954, Cowan et al 1954)

It has been suggested that the fluid crosses the diaphragm either through normal lymphatic channels (Rubin et al 1944, Lawson 1950) or through some abnormal defect in the diaphragm and its pleural and peritoneal coverings There are certain objections to the lymphatic route

(1) Although experimental studies have shown that the ascitic fluid can reach the subpleural lymphatics, they have not demonstrated how it can reach the pleural space (Higgins and Graham 1929)

(2) It does not explain why the hydrothorax is usually on the right side

(3) If ascitic fluid can pass so easily into the pleural space through normal lymphatic channels, a hydrothorax should invariably accompany ascites, but Meigs's syndrome is rare compared with ovarian tumours causing ascites alone, and hydrothorax with ascites due to cirrhosis of the liver is rare compared with cirrhosis causing ascites alone

It seems more likely that the ascitic fluid passes into the pleural space through some abnormal defect in the diaphragm and its serous coverings In the published cases of cirrhosis of the liver with ascites and recurrent massive hydrothorax the sequence of clinical events strongly suggests the presence of such a communication, Frothingham's (1942) case can hardly be explained in any other way In two other cases the syndrome has been proved to be due to a diaphragmatic defect in one the diaphragm had been ruptured by a recent motor car accident (Goodman 1937), in the other, three holes were found in the right hemidiaphragm at necropsy, each about 5 mm in diameter and thought to be congenital (Puech and Ratié 1933) In all the other published cases examined at necropsy the diaphragm was macroscopically intact These diaphragmat defects were relatively large and visible on macroscop examination of the diaphragm The communication in the present patient was very small and would not have been seen by ordinary macroscopic examination. This may be why such defects have not been reported before in connection with hydrothorax and ascites They have, however, been described in those cases in which from a pneumoperitoneum had passed through a def in the diaphragm to produce a spontaneous pneu thorax Only two of the published cases have been f and come to necropsy, in one of these there was a ble like projection on the pleural surface of the diaphr communicating with a hole 2 mm in diameter on the peritoneal surface (Yannitelli et al 1949) Similar ble have been seen at thoracoscopy (Laird 1945, Ross Farber 1951, Repa and Jacobson 1951)

Crofts (1954) expressed the opinion that most of the cases are due to a congenital diaphragmatic defect ca by the failure of deposition of single or multiple mu bundles The peritoneum lying under the defect is for through the gap by the raised intra abdominal pres and the pleura lying over the gap is raised to form a bl After it has ruptured, a bleb is no longer visible macroscopic examination (Macklin 1937)

It is likely that a similar mechanism operated in t present case of hydrothorax complicating ascites Th was no initially patent congenital communicati because there was at first ascites without a hydrothor The intra-abdominal pressure was sufficiently raised require repeated aspirations of ascitic fluid The hyd thorax developed suddenly Presumably the diaphrag and its coverings were ruptured by a further increase intra abdominal pressure due to coughing or strain We suggest that other cases of massive hydrotho complicating ascites due to cirrhosis of the liver and least some cases of Meigs's syndrome develop in way The present case makes it clear that the defect the diaphragm can be invisible to careful macrosco examination and yet allow a massive hydrothorax accumulate

## Summary

A case of recurrent massive hydrothorax complicat ascites due to cirrhosis of the liver was shown to be to a minute acquired defect of the right hemidiaphrag

It is suggested that at least some cases of massive hy thorax complicating ascites, including Meigs's syndro may have a similar mechanism

We wish to thank Dr James Dow for permission to publ

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## Preliminary Communication

# HYPOGLYCÆMIC EFFECT OF IMERCAPROL (BAL) IN BURNED PATIENTS AND IN DIABETICS WITH INSULIN-RESISTANT HYPERGLYCÆMIA

### urned Patients

THESE investigations began in 1950 after the chance iding of glycosuria in a patient recovering from burns. nce then 15 severely burned patients have been served to develop hyperglycæmia and glycosuria but t acetonuria, about five days after their injury when rce-fed to offset the expected loss of weight. Abnormal rbohydrate metabolism lasted days, weeks, or months, e duration being shorter in children than adults. The normality seems to be related at first to increased renocortical activity.[1] 6 patients with it showed creased excretion of urinary corticoids and depressed sinophil counts over the first five days in hospital mpared with other force-fed burned patients who did t develop hyperglycæmia, and with force-fed controls bed.

Of the 15 burned patients with hyperglycæmia 7 covered from their diabetes or died before further vestigations could be made. Various tests were made the remainder for comparison with other subjects. ucose tolerance tests with glucose 50 g by mouth were ade. Glucose-insulin (glucose 50 g by mouth and travenous insulin 5 units) tests were undertaken on e succeeding day, to investigate insulin resistance own to be related to increased adrenocortical activity.[2] nce the breakdown of glucose produces keto acids ood keto acid levels[3] were also estimated in these tests ble I). It seems that the insulin resistance of the abetic state in burned patients was most pronounced thin three weeks of injury and less from three to rteen weeks after injury, and that the diabetes was ulin-sensitive if it lasted over thirteen weeks. This t finding may be related to the damage observed in e β-cells of the pancreas of animals made diabetic by olonged sustained hyperglycæmia.[4]

The blood keto acid levels in burned patients with perglycæmia were raised and altered after the administation of glucose either alone or with insulin (table I). ese findings raised the possibility that the derangement their carbohydrate metabolism is associated with a ult at some point other than or in addition to the itial reactions whereby glucose enters cell metabolism.

It has been suggested that the effects of increased renocortical activity in animals may be related to altered thiol (SH) metabolism.[5-7] Since several SH enzyme systems take part in glycolysis and the Krebs cycle, and because it had been reported that intravenous glutathione reduced hyperglycæmia caused by corticotrophin,[8] it was decided to study the effect of dimercaprol (BAL), another SH compound, on the glucose tolerance of burned patients and of burned patients under treatment with corticotrophin. Dimercaprol 250 mg in oil was given intramuscularly at the start of a glucose tolerance or a glucose-insulin tolerance test. The results are shown in table I.

It seems that the single injection of dimercaprol slightly improved glucose tolerance in the hyperglycæmic burned patients when given alone in the early phase of greatest insulin resistance and when given with insulin from three to thirteen weeks after injury. In these patients the blood keto-acid levels showed a smaller rise an hour after the start of tests involving dimercaprol than in corresponding tests without dimercaprol. Subsequent experiments on hydrocortisone-treated rats confirmed the rise in blood keto acid levels[9-11] and chromatographic techniques indicated that pyruvate was the keto acid involved.

TABLE II—EFFECTS OF DIMERCAPROL IN DIABETICS

| Case no | Age | Sex | Insulin (units) |  | Glycosuria (g per day) |  |  | Average blood-sugar (mg per 100 ml.) |  |  |
|---|---|---|---|---|---|---|---|---|---|---|
|  |  |  | Av daily requirement | Dose in trial | Before dimercaprol | 3rd day of dimercaprol | After dimercaprol | Before dimercaprol | 3rd day of dimercaprol | After dimercaprol |
| 1 | 36 | F | 320 + | 320 | (> 2%) | (Trace) | (> 2%) | 150 | 110 | 400 |
| 2 | 36 | F | 280 + | 80 | 53 | 15 | 78 | 284 | 80 | 265 |
| 5 | 18 | M | 120 | 100 | 38 | 10 | 48 | 292 | 182 |  |
| 6 | 27 | M | 100 | 90 | 78 | 32 | 82 | 306 | 279 |  |
| 7 | 26 | F | 100 | 70 | 100 | 27 | 108 | 181 | 205 | 180 |
| 3 | 60 | F | 33 | 28 | 24 | 20 | 16 | 270 | 211 |  |
| 4 | 33 | F | 24 | 24 | 43 | 51 | 37 | 314 | 271 | 355 |

### Diabetics

In view of the apparent action of a single dose of dimercaprol in the hyperglycæmic burned patients 7 diabetics were investigated in longer trials. Their day-to-day insulin requirements ranged from 24 to more than 320 units. In 2 cases the insulin requirements were sufficiently high to indicate insulin resistance. All the

TABLE I—MEAN BLOOD-SUGAR AND BLOOD KETO ACID LEVELS (MG PER 100 ML.) FASTING AND ONE HOUR AFTER STARTING THE VARIOUS TESTS

| Type of subject | No | — | Glucose tolerance |  | Glucose-insulin tolerance |  | Glucose-dimercaprol tolerance |  | Glucose-dimercaprol-insulin tolerance |  | Repeat glucose tolerance |  |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
|  |  |  | Fasting | 1 hr | Fasting | 1 hr | Fasting | 1 hr | Fasting | 1 hr | Fasting | 1 hr |
| rce-fed controls | 4 | Sugar | 81 | 129 | 86 | 94 | 81 | 133 |  |  |  |  |
|  |  | Keto-acids | 1·2 | 1·5 | 1·2 | 1·7 | 1·2 | 1·4 |  |  |  |  |
| rce-fed burned patients without hyperglycæmia | 4 | Sugar | 101 | 163 | 94 | 116 | 87 | 126 |  |  |  |  |
|  |  | Keto-acids | 1·1 | 1·3 | 1·2 | 1·5 | 1·2 | 1·4 |  |  |  |  |
| rned patients with hyperglycæmia: |  |  |  |  |  |  |  |  |  |  |  |  |
| Within 3 weeks of injury (2) or on corticotrophin (2) | 4 | Sugar | 135 | 289 | 136 | 275 | 145 | 216 |  |  | 133 | [illegible] |
|  |  | Keto-acids | 1·7 | 2·8 | 1·8 | 2·4 | 2·1 | 2·3 |  |  | 1·7 | 2·9 |
| 3-13 weeks after injury | 3 | Sugar | 175 | 320 | 150 | 216 | 140 | 240 | 169 | 231 | 174 | 299 |
|  |  | Keto-acids | 1·8 | 2·7 | 2·5 | 3·1 | 1·6 | 1·5 | 2·1 | 2·4 |  |  |
| More than 13 weeks after injury | 2 | Sugar | 161 | 380 | 165 | 100 |  |  |  |  |  |  |
|  |  | Keto-acids | 2·2 | 2·7 | 1·8 | 3·1 |  |  |  |  |  |  |

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patients were admitted to hospital and given a regulated diet and insulin The diet included 25 g of glucose with each of the four daily meals Glucose tolerance and glucose insulin tolerance, blood-sugar and blood-pyruvate levels, and the twenty four-hour urinary output of sugar were estimated in 6 patients After control periods lasting from two to five days the patients were given intramuscular dimercaprol 5% in oil 4 ml four times daily for three days and insulin Glycosuria and blood sugar levels were estimated Glucose insulin tolerance and blood pyruvate levels were estimated again within a few hours of the last injection of dimercaprol in 5 patients The effects of dimercaprol were greatest on the third day The results are shown in table II

In all but 2 cases the glycosuria diminished on the third day of treatment with dimercaprol and insulin The same trends were observed in the blood-sugar levels Preliminary studies of blood pyruvate levels showed high values an hour after insulin was given in the glucose-insulin tolerance tests, these values were lower after dimercaprol treatment

These studies were pursued further in case 2 On a diet excluding the supplementary glucose this patient excreted daily in her urine 11 g of glucose (average of thirty seven days) on insulin 280 units a day, 8 g of glucose (average of twelve days) on the same amount of insulin with 4 ml of dimercaprol 5% in oil daily, and 2 g (average of eight days) when the insulin was with 8 ml of dimercaprol daily

It therefore seems that dimercaprol given in conju tion with insulin may improve glucose tolerance in t circumstances of these investigations, especially patients whose high insulin requirements suggest insu resistance In the two studies made so far there h been no laboratory evidence of concomitant depress of adrenocortical activity It is recognised that t glycosuria of these patients may nevertheless h induced adrenocortical overactivity The intensity glycosuria during the control period was, however, so closely related to the effect of dimercaprol as was patient's insulin requirement Attempts are now be made to analyse the disturbance in glucose metabol which appears to be corrected by dimercaprol

The burned patients were studied at the Medical Col of Virginia, Richmond, Va The diabetics were studied Guy's Hospital through the kind coöperation of Dr C H wick, with Prof R H S Thompson, Dr B McArdle, W H H Merivale, and Dr C L Joiner, and the labora animals were studied in conjunction with Professor Thom and Dr M F S El Hawary

W J H BUTTERFIELD
O B E, M A Oxfd,
M D Johns Hopkins, M.R.C.P
Member, Medical Research Counc
Clinical Research Unit

Guy's Hospital, London

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# Medical Societies

## ROYAL SOCIETY OF MEDICINE

### Hormones and Cancer

A MEETING of the section of endocrinology was held on Feb 23, with Dr P M F BISHOP, the president, in the chair

SIR CHARLES DODDS, F R S, distinguished two periods of development leading to the present position The empirical period saw the establishment of gonadectomy as a palliative treatment in carcinoma of the prostate and breast Dating from 1930, the scientific period began with the isolation and characterisation of the steroid hormones and saw the establishment of their relationship with the gonads and adrenal cortex No single factor did more to advance our knowledge of the interrelationships of the endocrine glands, and the importance of pituitary trophic hormones, than the establishment by Selye of a reliable procedure for hypophysectomy of the rat Effective castration may be established directly by hypophysectomy or indirectly by the suppression of anterior-pituitary secretion

Huggins, using serum acid phosphatase levels, correlated prostatic growth with androgen production and used stilbœstrol to obtain clinical remission in carcinoma of the prostate by suppressing pituitary secretion Probably stilbœstrol treatment is also advantageous in 5–20% of cases of carcinoma of the breast, though here the rationale is hard to follow The improvements obtained are not permanent, and when neoplastic growth is renewed it no longer responds to administered hormones Huggins claims that this escape from control following gonadectomy is the result of hyperactivity of the adrenal cortex which can synthesise both œstrogens and androgens and he maintains that in such cases bilateral adrenalectomy gives a further period of control and some prolongation of life When, in turn, the clinical remissions obtained by these diverse methods disappear, the last ditch has been reached Presumably, in the absence of target organs, the secretion of pituitary trophic hormones is unopposed and these may exert some influence on somatic cells Data are insufficient to indicate whether hypop omy is justified Pearson has reported some improvement following hypophysectomy in a case carcinoma of the breast which no longer responded hormonal treatment, in this case the administration growth hormone stimulated the growth of both prim and secondary tumours A review of 37 cases of h physectomy suggests that results are best at the me pause and less satisfactory with advancing years W undifferentiated growths the response is better t with adenocarcinomas

It has proved impossible, throughout this work, forecast whether a given patient is likely to be by any course of treatment Quantitative methods for determination of steroids are notoriously diffic yet this is the most urgent need if reliable guides treatment are to be established

SIR STANFORD CADE described the hormonal treatm of cancer as a placebo or a palliative at its best T no cure was achieved, some temporary alleviation secured, and as a last resort any relief was good for patient One important result of the new approach the altered conception of cancer, whatever its as something dependent on and sustained by physiological processes It is established that tumo can be induced by œstrogens, but, to be effect the application must be long-continued Probably endogenous stimulation of neoplastic tissue must wise be continuous in application As the epithe tissues of the genitalia normally depend for their deve ment on œstrogens, it is not remarkable that malign forms of this tissue should respond to an œstroge background Ovariectomy by itself has a signific effect on disseminated carcinoma of the breast, 10-30% of patients survive from six to eighteen months, and few from three to five years The clinical use of androgens also has a palliative effect in such cases—especially on bony metastases—though the duration of this effect varies and there are undesirable side effects

The reason for bilateral adrenalectomy is that pro duction of steroid hormones continues after gonadectomy It is accepted that after the menopause the excretion ovarian hormone may remain active for many years and it is undoubtedly true that 17-ketosteroid production not zero in the castrate male Sir Stanford felt th bilateral orchidectomy and adrenalectomy gives effectiv ntrol of carcinoma of the breast and prostate only for a me—perhaps for two or three years—and he has no faith a lasting cure Furthermore the procedure has to be rried out blindly, without any indication whether or t the tumours are likely to be responsive He ha t found the histological differentiation suggested by uggins useful for this purpose and he strongly endorsed r Charles Dodds s plea for laboratory methods of ntrol. A remarkable feature of bilateral adrenalectomy the rate of improvement, objective signs such as lief of pain occurring within twenty four hours Post erative control has been achieved with cortisone alone ough the amounts required vary considerably and some tients need careful supervision In cases which hav me to necropsy no accessory adrenal tissue has been und.

After bilateral adrenalectomy and gonadectomy the cretion of pituitary trophic hormones is unopposed d it is conceivable that these may have a direct influence the behaviour of somatic cells. Though the mechanism ay be different the clinical effects of hypophysectomy e very similar to those following bilateral adrenalec my; and this treatment may be more effective in rcinoma of the prostate It is possible that hypophysec my may be also useful in other neoplasms such as elanoma and seminoma of the testes. Radical surgery n be justified only when secondaries are widely disminated and milder forms of treatment are no longer ective

Dr G L. Foss described the results of hormone erapy in different age groups of patients with carcinoma the breast Large doses of androgens (testosterone propionate testosterone phenyl propionate and methyl androstendiol) and of œstrogens (stilbœstrol) were administered and the results were analysed statistically Œstrogens were more effective in elderly patients and in general controlled growths in soft tissues Androgens were most useful in younger patients and more effective against osseous metastases The prognosis was more favourable in patients over 60 years

Dr IAN F SOMMERVILLE reported results following the intravenous administration of progesterone to cancer patients before and after bilateral adrenalectomy The excretion of pregnanediol under these conditions showed that the adrenal gland is not essential for this phase of progesterone metabolism

Dr A LOESER said that ovariectomy or adrenalectomy affected the growth of cancer cells merely by provoking the anterior pituitary to elaborate more thyrotrophic hormone If in advanced cancer œstrogens or androgens were given thyroid hormone should also be given, and thyroid hormone alone might be given after removal of the neoplasm, the maintenance dose being determined by the blood cholesterol level

Mr A G ELLERKER also reported finding some correlation between non toxic goitre and carcinoma of the breast and suggested that the thyroid hormone may act as an anticarcinogenic agent

Dr J G C SPENCER had studied W H O records and had found clear correlation between the incidence of goitre and cancer in the statistics of several countries He felt that thyroid activity was a factor of significance in cancer

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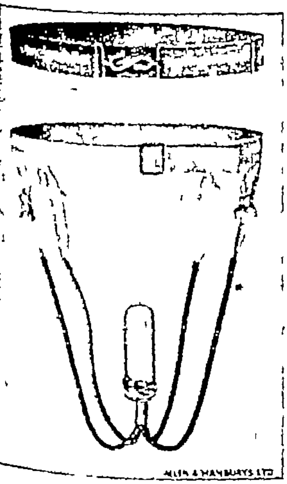
# New Inventions

## AGINAL PLUG FOR PROCIDENTIA IN ELDERLY WOMEN

For some years I have been attempting to devise a mfortable vaginal plug to act as a support to the omb in elderly women with procidentia who cannot tain a pessary and are too old or ill for operation. I ave now succeeded and have already seven very ateful patients who say they can walk long distances d are free from dragging pains and frequency of micturition when using this vaginal plug



The plug *is like a test tube and is inserted on rising and removed on going to bed It is made of* clear Perspex is unbreakable and easy to clean and does not perish. The belt and tapes are similar to those of the Napier cup-and stem pessary they are worn outside the undervest for comfort When an old lady has a sensible daughter who can use a needle and thread, I advise transferring the tape attachments to a boy s serpent buckle belt because this makes its fitting on and taking off a matter of seconds only It takes some time for the patient to get used to the appliance which should at first be used for only a few hours daily

I find it is a great help in all cases to prescribe 1 mixed gland tablet daily from Mondays to Fridays—e g Mepilin (B.D.H) Hormostergon (Polypharma) Myxogen (Organon) Menopax forte (Clinical Products) or 'Formandren (Ciba) A course of one of these tablets daily will cause the vaginal walls to become less degenerate tender and thin, and emotionally the patient feels happier

The ages of these seven patients are 89 81 80 73 72 55 and 40 The patient aged 40 is wearing a plug as a temporary measure while awaiting operation The patient aged 55 has been under treatment for cancer of the breast for some months and will be operated on later if all goes well. The patient aged 72 first reported to me with an impacted Napier cup and-stem pessary causing a vesicovaginal fistula. I removed the stem from the injured bladder wall and six weeks later repaired the fistula. She is now very happy with a vaginal plug In the patient aged 73 the procidentia was so wide and large that the plug kept turning right round and coming out An especially large plug was made—almost jam pot size—and is a complete success.

The older the patient with procidentia, the greater seems the success. All those aged 89 81 80 73 and 72 are especially grateful for the benefits derived from its use

The plug can be cleaned by dipping it in boiling water glycerin can be used as a lubricant but is seldom necessary The rubber attachments and the rubber stem immediately below the tube tend to perish and require renewal yearly The perspex tube is unlike rubber non irritating hence douching is seldom required There is no danger of impaction or of fistula as is the case with the Napier cup-and stem pessary and even ulcerated cervices improve and can heal while this plug is in place

The older the patient and the greater the prolapse the more helpful is the plug and the deeper the patient s gratitude

This apparatus is not always successful in apparently suitable cases, but these number less than one in four

The vaginal plug can be supplied by Messrs Allen & Hanburys, Wigmore Street London, W 1

London, W 1

MCKIM MCCULLAGH
F.R.C S.E.

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[1] See *Lancet* 1954, ii 1315

# THE LANCET

*LONDON SATURDAY, MARCH 5 1955*

## Horror Comics

Concern over the bad effect on children of so-called comic books was awakened in this country several years ago[1] and has been mounting steadily. It has now led to the introduction of a Parliamentary Bill to curb this type of publication. With the Bill now in committee, there will be more than usual interest in Dr Wertham's authoritative study[2] of "horror comics" in the United States of America. After a seven-year investigation Wertham concluded that the only way to fight this social evil is through the law, which he has described as "the best instrument of adult education." It is sobering, therefore, to find that he has failed to secure any action, and that some of the arguments used against our own Bill at its second reading on Feb. 22 contributed to his defeat in the U.S.A.

His book is shocking, both because it reveals an appalling state of affairs, and also because of the violence of his own feelings. He produces apparently incontrovertible evidence, but he batters the reader with it, and those psychiatrists and others who do not share the extremity of his views are belaboured as savagely as the promoters of the comic-book industry themselves. But it would of course be wrong to dismiss this work because the author's burning moral indignation has led him into ungentle ways and disturbed his judgment. He has with great devotion, courage, and integrity, revealed a calamitous state of affairs. In the U.S.A. the output of horror comics, as distinct from "comic strips" which are less noxious, is conservatively estimated at 60 million per month. Not only do the children and some young adults trade the comics among themselves, but they tend to live with them, read them again and again, and generally treat them as the great reality of life. With copious extracts and illustrations, Wertham shows how horror comics are preoccupied with blood, lust, violence, murder, cruelty, perversion, and racial intolerance. He has even traced an epidemiology, showing how the industry has quickly passed through phases of murder and violence, sex, and sexual murder with violence and how it has been "retooled for illiteracy." He shows how the comics are influencing both boys and girls, and traces new trends in juvenile crime with an early recognisable comic-book flavour.

How much does all this apply to our own country? Nobody would claim that the horror-comic menace is as serious here; but a recent exhibition by the National Union of Teachers of comic books found in Britain has shown the threat to be far from negligible. An intelligent London grammar-school boy of 13 was asked within the last week to give an opinion on the matter, and proved both knowledgeable and informative. In his school, he thought, in each of the three lowest forms about two boys were purveyors of horror comics, but most of the boys did not touch them. Higher up the school interest waned. He volunteered a classification into grade I (the worst), murder and sex; grade II, murder and violence; and grade III, just murder. He exonerated from blame what he described as "standard British comics," but the effect of the others was "shockingly awful." Most of the horror-comic books, he said, were of American origin, though possibly printed in the United Kingdom; but he claimed to know of at least four series of comics produced in this country which are as bad in their morals and effects, the only difference being that the language does not "contain so much slang."

The anti-comics campaign has been defeated in America not only by the complexities of State law but by other factors deserving study, including the public endorsement of horror comic books by some psychiatrists. (The Kefauver Senate Crime Committee named two well-known child psychiatrists and two educationists as having been employed by the comic-book industry, but Wertham gives no names, and the nature of their employment is only hinted at.) The grounds alleged for endorsement of comics by psychiatrists include the argument that comics allow the child to "let out his aggression," but in fact the consensus of psychiatric opinion is that they stimulate and tend to formalise his aggression and deny him the civilising experience of controlling his aggression himself and of diverting it on to socially acceptable objectives. (To quote a crude example, it is better for a boy to "attack" his algebra problems than the six-year-old girl next door.) Among the unthinking the publishers of comics win further support by claiming that their products teach that "crime does not pay"; but the lesson that actually emerges is generally that violence is the most important of values, that it can be conquered only by greater violence, and that the worst evils are to make a mistake and to be the weaker party. The arguments in favour could hardly have succeeded but for the belief of many well-intentioned people that horror comics will harm only the emotionally unstable or disturbed child. To say this is as futile as to say that a motor car will only harm the child who does not understand traffic; and Wertham gives us convincing evidence that the argument is also false—that comics not only create a dependence on comics but inculcate criminal ideas, provide courses of instruction in criminal behaviour, and advertise the sale of the necessary weapons and tools. To mix the metaphor, it is as though some motor cars were to pursue children on to the pavement, trap them, and "take them for a ride."

But (it is said) to ban comics interferes with the right of free speech and with the freedom of the press. Who shall be the arbiter of morals? Echoes of these arguments were heard at Westminster last week. Are the police trained for this sort of thing? Will not a publishers' code do what is necessary? Wertham shows that in the United States a code has been not only useless but dangerous, because it gave a sense of false security. As for curbing freedom, he inquires, freedom for what and for whom? Certainly not freedom for the child who is destined to become a slave to the horror comic. There is some parallel here with the argument that the child labour laws of the 19th century were wrong because they denied to the child "the right to work in the coalmine," or that public health regulations are wrong because they deny

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[1] See *Lancet*, 1950, i, 1005.

[2] Seduction of the Innocent. By Fredric Wertham, M.D., sometime senior psychiatrist for the Department of Hospitals in New York City. London: Museum Press. 1955. Pp. 407. 21s.

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## Horror Comics

CONCERN over the bad effect on children of so called comic books was awakened in this country several years ago[1] and has been mounting steadily It has now led to the introduction of a Parliamentary Bill to curb this type of publication With the Bill now in committee, there will be more than usual interest in Dr WERTHAM's authoritative study of "horror comics" in the United States of America After a seven year investigation WERTHAM concluded that the only way to fight this social evil is through the law, which he has described as 'the best instrument of adult education.' It is sobering therefore to find that he has failed to secure any action and that some of the arguments used against our own Bill at its second reading on Feb 22 contributed to his defeat in the U.S.A

His book is shocking, both because it reveals an appalling state of affairs and also because of the violence of his own feelings He produces apparently incontrovertible evidence but he batters the reader with it, and those psychiatrists and others who do not share the extremity of his views are belaboured as savagely as the promoters of the comic book industry themselves But it would of course be wrong to dismiss this work because the author's burning moral indignation has led him into ungentle ways and disturbed his judgment He has with great devotion courage and integrity, revealed a calamitous state of affairs. In the U.S.A the output of horror comics as distinct from "comic strips' which are less noxious, is conservatively estimated at 60 million per month Not only do the children and some young adults trade the comics among themselves, but they tend to live with them, read them again and again and generally treat them as the great reality of life With copious extracts and illustrations, WERTHAM shows how horror comics are preoccupied with blood, lust, violence murder cruelty, perversion, and racial intolerance He has even traced an epidemiology showing how the industry has quickly passed through phases of murder and violence sex, and sexual murder with violence, and how it has been 'retooled for illiteracy He shows how the comics are influencing both boys and girls, and traces new trends in juvenile crime with an early recognisable comic book flavour

How much does all this apply to our own country? Nobody would claim that the horror comic menace is as serious here, but a recent exhibition, by the National Union of Teachers of comic books found in Britain has shown the threat to be far from negligible An intelligent London grammar-school boy of 13 was asked within the last week to give an opinion on the matter and proved both knowledgeable and informative In his school, he thought in each of the three lowest forms about two boys were purveyors of horror comics but most of the boys did not touch them. Higher up the school interest waned He volunteered a classification into grade I (the worst) murder and sex grade II, murder and violence and grade III, just murder He exonerated from blame what he described as standard British comics but the effect of the others was 'shockingly awful Most of the horror-comic books, he said were of American origin though possibly printed in the United Kingdom but he claimed to know of at least four series of comics produced in this country which are as bad in their morals and effects, the only difference being that the language does not ' contain so much slang

The anti comics campaign has been defeated in America not only by the complexities of State law but by other factors deserving study, including the public endorsement of horror comic books by some psychiatrists (The Kefauver Senate Crime Committee named two well known child psychiatrists and two educationists as having been employed by the comic book industry, but WERTHAM gives no names and the nature of their employment is only hinted at) The grounds alleged for endorsement of comics by psychiatrists include the argument that comics allow the child to let out his aggression but in fact the consensus of psychiatric opinion is that they stimulate and tend to formalise his aggression and deny him the civilising experience of controlling his aggression himself and of diverting it on to socially acceptable objectives (To quote a crude example it is better for a boy to 'attack his algebra problems than the six year old girl next door) Among the unthinking the publishers of comics win further support by claiming that their products teach that crime does not pay but the lesson that actually emerges is generally that violence is the most important of values that it can be conquered only by greater violence, and that the worst evils are to make a mistake and to be the weaker party The arguments in favour could hardly have succeeded but for the belief of many well intentioned people that *horror comics will harm only* the emotionally unstable or disturbed child To say this is as futile as to say that a motor car will only harm the child who does not understand traffic, and WERTHAM gives us convincing evidence that the argument is also false—that comics not only create a dependence on comics but inculcate criminal ideas provide courses of instruction in criminal behaviour and advertise the sale of the necessary weapons and tools To mix the metaphor, it is as though some motor cars were to pursue children on to the pavement, trap them and take them for a ride

But (it is said) to ban comics interferes with the right of free speech and with the freedom of the press Who shall be the arbiter of morals? Echoes of these arguments were heard at Westminster last week Are the police trained for this sort of thing? Will not a publishers code do what is necessary? WERTHAM shows that in the United States a code has been not only useless but dangerous because it gave a sense of false security As for curbing freedom he inquires freedom for what and for whom? Certainly not freedom for the child who is destined to become a slave to the horror comic There is some parallel here with the argument that the child labour laws of the 19th century were wrong because they denied to the child the right to work in the coalmine, or that public health regulations are wrong because they deny the child the right to catch typhoid fever No responsible citizen will give away civil liberties for nothing, but we must not protect the liberty of the adult to make money as he pleases at the cost of failing to protect the child's freedom to grow up without lasting deformity of character

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[1] See *Lancet* 1950, i 1003

[2] Seduction of the Innocent By FREDRIC WERTHAM M.D, sometime senior psychiatrist for the Department of Hospitals in New York City London: Museum Press 1955 Pp 407 21s

## Idiopathic Thrombocytopenic Purpura

IT used to be thought that idiopathic thrombocytopenic purpura was a form of hypersplenism, the spleen sequestrated and destroyed the circulating platelets, and the megakaryocytes in the bone-marrow multiplied in an effort to replace the loss This hypothesis was supported by the effect of splenectomy, which was usually followed by return of the platelet-count to normal and disappearance of the purpura But from the first it was realised that this explanation was incomplete Splenectomy unaccountably failed to relieve some patients in whom the diagnosis was firmly established, while in others the platelet-count increased at first, but fell later—sometimes without recrudescence of the purpura Moreover, the severity of the bleeding into the skin or from mucous membranes did not necessarily correspond to the level of the platelet-count These anomalies, and doubts about the necessity for, or the timing of, splenectomy in individual patients, have stimulated a search for other factors in the pathogenesis and course of the disease Recent work on platelet agglutinins and lysins shows that the search is well justified

The idea of platelet-antibodies stems from observations on guineapigs by BEDSON,[1] who prepared an antiplatelet serum which caused thrombocytopenia and damaged the endothelium of the capillary blood-vessels Interest in this aspect of purpura has been re-awakened by two researches Firstly, ACKROYD [2] showed that the thrombocytopenic purpura caused by 'Sedormid' is due to the development of an antiplatelet factor in the blood Secondly, EVANS et al [3] noted that some patients with acquired hæmolytic anæmia also had thrombocytopenia Since the hæmolytic anæmia was known to be caused by antibody destruction of red cells, they thought that the thrombocytopenia might similarly be due to an antibody, and they detected platelet-agglutinating factors in the blood of these patients and of some with idiopathic thrombocytopenic purpura EVANS et al considered that the spleen acted more as an antibody-producer than as a "slaughterhouse" of red cells and platelets They also pointed out that children born to women who at the time had thrombocytopenic purpura often had transitory thrombocytopenia, which suggested that a platelet destroying factor had passed across the placenta STEFANINI and DAMESHEK,[4] and others, have worked out techniques for transfusing platelets and following their fate in recipients They found that normal platelets transfused into patients with a low platelet-count due to aplastic anæmia or leukæmia survived for two to five days, whereas platelets transfused into patients with idiopathic thrombocytopenic purpura survived for from half an hour to twenty-four hours HARRINGTON et al [5] made the converse experiment of transfusing blood from patients with idiopathic thrombocytopenia into healthy people, and showed that in many this caused temporary thrombocytopenia They also detected platelet agglutinins in the blood of 21 out of 31 patients with idiopathic thrombocytopenic purpura, and in 4 of these the agglutinins acted against the patient's own platelets TULLIS [6] found that serum from some patients with such purpura caused agglutination and even lysis of normal platelets in the presence of complement These, and similar reports, seemed to confirm that a circulating antiplatelet-antibody was present and was detectable in a fair proportion of cases of idiopathic thrombocytopenic purpura, and this presumably was responsible for the thrombocytopenia and the purpura

Further experience has yielded results which spoil this attractively simple picture HARRINGTON et al [5] noted that thrombocytopenia was still induced in healthy people by blood from patients whose platelet-count had reverted to normal after splenectomy Further search revealed platelet agglutinins in the blood of patients without purpura who had been transfused or who had been pregnant, and STEFANINI et al [7] described platelet-agglutinins in the blood of healthy people who had never been transfused or been pregnant The techniques of demonstrating platelet-agglutinins have proved difficult and unreliable, and there is much difference of opinion about the interpretation of results The reduction in the platelet-count of healthy people transfused with blood from patients with idiopathic thrombocytopenic purpura is also not specific, thus STEFANINI et al [8] found that transfusion of normal plasma causes reduction of platelets, and the only difference with plasma from patients with thrombocytopenic purpura is that the effect sometimes lasts longer ACKROYD [9] concludes that the extent to which idiopathic thrombocytopenic purpura is due to an antiplatelet factor is not easily judged, though there is strong evidence of such a factor in the blood of some patients with the disease

Accordingly, the clinician cannot look to information about platelet-agglutinins to help him in deciding whether splenectomy is advisable, or whether cortisone or corticotrophin should first be tried But experience over the years has helped to clarify the division of idiopathic thrombocytopenic purpura into an acute type, which does not often call for splenectomy, and a chronic type, in which sooner or later splenectomy will probably be necessary The acute cases, which are very alarming, were formerly treated by emergency splenectomy, but the results were often disappointing The present practice of watchful waiting has shown that the condition often remits spontaneously after a period varying from a few weeks to three or four months, in some instances the disorder eventually becomes chronic, but in occasional tragic cases the patient dies from uncontrollable hæmorrhage that is uninfluenced even by splenectomy Cortisone may help to tide over the waiting period, platelet transfusions have been given, but have severe limitations In the chronic cases the platelet-count is persistently

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1 Bedson S P *J Path Bact* 1022 25, 91
2 Ackroyd J F *Clin Sci* 1949 8 269
3 Evans R S Takahashi K. Duane R. T, Payne R Liu C K *Arch intern Med* 1951 87 48
4 Stefanini M. Dameshek, W *New Engl J Med* 1953 248 797
5 Harrington W J Sprague C C, Minnich V Moore C V A Dubach R *Ann intern Med* 1953, 38 433
6 Tullis J C *New Engl J Med* 1953 249 591
7 Stefanini M, Pitman G I Dameshek W Chatterjea J B Mednicoff I B *J Lab clin Med* 1953 42 723
8 Stefanini M Dameshek W Chatterjea, J B, Adelson, E Mednicoff I B *Blood,* 1953 8, 26
9 Ackroyd J F *Brit med Bull* 1955 11, 28
10 See *Lancet* 1953 ii, 605

r for many months, and the purpura tends to vary nto independently. Splenectomy is still the treat nt of choice, and the timing of this operation pends greatly on such considerations as whether the morrhages are persistent or damaging, whether patient is likely to become pregnant, or whether central nervous system is involved. Unfortunately STEFANINI and DAMESHEK[11] point out, it is still possible to predict whether the disorder will pond to splenectomy, but in at least two thirds of es the results of operation are satisfactory. In ldren idiopathic thrombocytopenic purpura tends be milder than in adults, but more cases are acute th the risk of serious complications in the first nth of the illness. KOMROWER and WATSON[12] port that of 28 cases in children aged 6 years or less fewer than 24 presented as acute cases, 12 with ere and 12 with mild bleeding. 6 of the children th severe bleeding died, but the other 18 recovered mpletely without treatment. In the chronic cases children the onset is less dramatic, and symptoms d to persist in an irregular fashion for more than months. KOMROWER and WATSON agree that in acute cases splenectomy is hazardous, and they efer treatment with corticotrophin or cortisone for least the first month after onset. For the chronic es splenectomy should be considered after six onths, but the necessity for this depends on the ability the disease is causing.

The successful management of idiopathic thrombotopenic purpura in children or adults still depends accurate diagnosis and on clinical assessment of the ndition and prognosis, as much as on information m clinical pathology. The detection of platelet glutinins is not yet a helpful laboratory test, but chnical refinements may make it so.

## Peptic Ulcer and the Brain

VAGAL section may be indicated in cases where the astomosis ulcerates after comprehensive gastric section for duodenal ulcer, and as a supplement to e Billroth I operation for duodenal ulcer it may ure against recurrence.[13] A report from the Mayo linic[14] indicates that, though gastric resection is e operation of choice for ulceration after gastro terostomy, vagotomy with a low mortality of 1% ives excellent results in 70% of patients with stomal ker after partial gastrectomy; indeed compared with e few cases submitted to gastric reresection which ere followed up, vagotomy was apparently more effec ive. WELLS[15] has reported the outcome of vagotomy 25 patients with ulceration after partial gastrectomy nd 14 after gastro-enterostomy: two-thirds of the section group were free from trouble after three ears, but the results in the gastro-enterostomy group ere disappointing since ulceration recurred in 10. ELLS considers that vagotomy is worth trying in e gastrectomy group since it is safer than further section. There are occasions when removal of yet ore stomach is well nigh impossible: vagal section s then a last resort.

Occasionally peptic ulceration defies all surgical endeavours. PRIESTLEY et al.[16] mention a patient who had five operations and ultimately required total gastrectomy. In such cases the underlying factors can hardly be gastric, since ulceration continues to recur after most of the stomach has been removed. WALTERS et al.[14] suggest that the continual presence of free HCl in the stomach or stomach remnant is important, and base their surgical approach to recurrent ulceration on its elimination. FRENCH et al.[17] have found that in monkeys stimulation of the hypothalamic area induces secretion of HCl. Section of the vagus nerve might have been expected to stop this response if their experiments had not also pointed to an extravagal pathway from the posterior hypothalamus through the pituitary adrenal system: stimulation caused a delayed secretion which was blocked only by adrenalectomy.[18] If acid is a factor in ulceration, and if stress stimulates the hypothalamus, this might explain the rare recurrence of ulceration after adequate gastric resection followed by vagotomy. FRENCH et al.[19] have induced in monkeys ulceration in prepyloric and postpyloric areas by protracted stimulation (thirty to seventy days) of the medial diencephalic axis from preoptic to postmamillary regions. This circumstantial evidence does not prove that a similar mechanism operates in man. But clinical observation caused CUSHING[20] to consider the rôle of stress and its impact via interbrain to midbrain and so on to the vagal centres in the medulla. His interest was aroused by two cases in which acute gastric or duodenal perforations followed craniotomy for cerebellar lesions. The several perforations were located in areas of erosion—in the stomach in one case and in the duodenum in the other. Ulcers that follow operations on the brain are apparently of two types: one is characterised by diffuse petechiae and even gross hæmorrhage, and the other by gelatinous softening, erosion, and perforation.[21] DAVIS et al.[22] have found that the incidence of perforation or hæmorrhage after 7000 neurosurgical operations was 0.7%, but after craniotomies (943) and also after suboccipital craniectomies (350) it was about 2.5%. 8 patients in their series had pre-existing gastro-intestinal trouble; after operation all 8 were seriously ill because of hæmatemeses, and some of these died from this cause. In some cases gastro-intestinal hæmorrhage ensued even when the operation had not been on the central nervous system—for example, on the autonomic nerves. Moreover, as CUSHING knew, disease of the central nervous system without neurosurgical trauma may be associated with perforation or hæmorrhage. WATSON and NETSKY[23] describe 6 such cases and refer to 38 previously reported in which the patient died from one of these complications. In 30 of the total of 44 cases the neurological disorder involved the hypothalamus.

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1. Stefanini, M., Dameshek, W. *Ann. Rev. Med.* 1954, 5, 87.
2. Komrower, G. M., Watson, G. H. *Arch. Dis. Childh.* 1954, 29, 502.
3. Capper, W. M., Welbourn, R. B. *Lancet*, 1954, ii, 105.
4. Walters, W., Chance, D. P., Berkson, J. *Surg. Gynec. Obstet.* 1955, 100, 1.
5. Wells, H. W. *Lancet*, 1954, i, 509.

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17. French, J. D., Longmire, R. L., Porter, R. W., Movius, H. J. *Surgery*, 1953, 34, 621.
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19. French, J. D., Porter, R. W., Cavanaugh, E. B., Longmire, R. L. *Arch. Neurol. Psychiat.* 1954, 72, 267.
20. Cushing, H. *Surg. Gynec. Obstet.* 1932, 55, 1.
21. French, J. D., Porter, R. W., von Amerongen, F. K., Raney, R. B. *Surgery*, 1952, 32, 395.
22. Davis, R. A., Wetzel, N., Davis, L. *Surg. Gynec. Obstet.* 1955, 100, 51.
23. Watson, J. MacD., Netsky, M. G. *Arch. Neurol. Psychiat.* 1954, 72, 426.

This association between brain and gut is still sometimes overlooked, though SCHIFF[24] observed it in dogs and rabbits as long ago as 1846 Four years previously CURLING[25] had reported duodenal ulceration after burns—a sequence which BROWN-SÉQUARD[26] tried to explain neurologically Neurological manifestations after severe burns have often been reported, and necropsy has revealed œdema, hæmorrhages, and purpura in the brain, changes in ganglion cells, and demyelination MADOW and ALPERS[27] recorded this state in 2 patients who died twelve and sixteen days after being burnt, and the patient who died after twelve days also had Curling's ulcer of the stomach Yet, though brain lesions may play a part in the genesis of ulcers, secretion of HCl, stimulated by the hypothalamus, can hardly be the whole cause, since ulceration of œsophagus[21 28] and colon[21] has also been found in association with cerebral disorders

## Annotations

### AIR IN THE INFANT'S ALIMENTARY TRACT

PARENTS of small babies are often puzzled as to where all the wind comes from Usually they are assured that it has been swallowed, but the question of when it is swallowed has never been satisfactorily answered It is commonly believed that babies swallow air when they have nothing else to swallow, and that a hungry baby will gulp down large quantities of air to try and relieve his pangs It has even been suggested[29] that some air is ingested with every inspiration, but as little as 0 1 c cm of air swallowed with each breath would mount up to more than 5 litres per day

Gerber[30] has now described observations which suggest that air is not easily swallowed by infants unless they are swallowing fluid at the same time Gerber studied a series of babies whose ages ranged from 12 days to 9 months, and also two older children, one aged 18 months and the other aged 6 years A plain radiograph of the abdomen was taken after 4–8 hours' fasting and the amount of gas in the stomach was estimated Next the infants were allowed to suck on an empty bottle for 30 minutes and a further radiograph was taken Finally, they were given from a half to four ounces of milk and a final radiograph was taken There was little gas in the stomach of fasting infants, and there was practically no change after 30 minutes' sucking on an empty bottle, whereas after the milk feed there was moderate to great increase Gerber estimated that the babies swallowed two to three times as much air as fluid during a feed A further observation confirmed that the air was swallowed and did not appear as the result of decomposition of food or by diffusion from the blood Three babies were given a small amount of milk by bottle, and subsequent radiographs showed the normal stomach gas bubble On another occasion they were given the same amount of milk through a gastric tube, and no gas-bubble could be seen on the radiographs In a third test Gerber passed gastric tubes on three infants and placed the free ends under water There was an immediate bubbling of gas as the stomach emptied but no further escape with expiration, which suggested that air was not being ingested with breathing

Nevertheless there seems to be no doubt that the newborn baby swallows air as the stomach and small bowel fill with gas shortly after birth and before any are given Further, the infant with œsophageal without tracheo œsophageal fistula does not have gas in the bowel, and so diffusion from the blood str would not explain the rapid distension of the no baby's gastro-intestinal tract

All too often in medicine opinions tend to crysta into accepted fact The belief that hungry babies swa air has hardly been questioned Those who find Ger conclusions unacceptable will now have to prove t case, and not merely state it

### HEREDITY AND RHEUMATIC FEVER

WE know that anyone who has had an attack rheumatic fever is liable to have further attacks, that the hazard may be diminished by long term ch prophylaxis with penicillin or the sulphonamides. present such prophylaxis cannot be rationally ap before the first attack, since there is no means recognising susceptibility

Infection, possibly recurrent, by the group A β-ha lytic streptococcus is established as an essential ca the disease, and factors influencing the dissemin of the streptococcus will materially affect the inci of rheumatic fever This has been well shown in y adults who have been segregated and crowded toge as on call up to the Services,[1] when epidemics of str coccal infection have resulted in minor epidemi rheumatic fever We do not know why some pe react to streptococcal disease in this way, but there increasing evidence that susceptibility to rheumatic fe is inherited Family studies,[2 3] including pedigree rheumatic families,[4 5] and records of identical and n identical twins,[6 7] have suggested that heredity involved, but environmental influences have not b satisfactorily distinguished from genetic influences, has the mode of inheritance been clarified Interpreta of results is not easy Usually families are chosen study because they include an affected child, and al ance must be made for this weighting of the data comparisons with control families chosen on some ot basis Secondly, rheumatic fever and rheumatic he disease are diagnosed clinically, and different obser will not always agree on criteria Thirdly, informat on rheumatic disease among the parents' relatives is always accurate Finally, the children studied must followed up for many years

Wilson and Schweitzer[8] in New York have descr a long-term study in which an attempt was made overcome these difficulties From their earlier invest tions[9] these workers had concluded that susceptib to rheumatic fever was inherited as a simple rece trait, and their latest investigation was designed confirm that hypothesis The families were brou under observation through a parent who was seen du childhood at a pædiatric heart clinic on account rheumatic or congenital heart disease, in addition, so of the brothers and sisters of these patients were includ together with some patients admitted to an obstetr hospital who were found to have rheumatic heart-disea The kin of both parents were examined with some ca The children were followed continuously over year and the incidence of rheumatic disease among them wa related to the probable genetic constitution of the parents assuming single recessive gene transmission The observed ddence agreed well with that theoretically expected m this hypothesis Thus according to the hypothesis ere both parents were rheumatic and therefore both sumably homozygous for the rheumatic gene all the ldren would be likewise homozygous and develop disease, and in fact in eight such families 14 of the children were rheumatic. On the other hand if one ent had no family history of rheumatic fever he might assumed to be a homozygous negative so if the tner were rheumatic all the children would be erozygous and although carriers of the recessive trait uld not themselves show the disease Among 399 h children only 2 cases of rheumatic fever were erved This evidence is persuasive But Wilson and weitzer assume 100% penetrance of the trait which uld require universal exposure of the children to urrent streptococcal infection and the families were satisfactory economic status so it is unlikely that this dition was fulfilled In addition the general decline the incidence of rheumatic disease would not have en place if the disease were determined by a purely editary cause with such a high degree of penetrance e in six of the children had not attained the age of 6 rs and an even larger proportion had not passed the eptible age period, the total incidence is therefore ely to exceed that required by the hypothesis of a essive gene especially if less than 100% penetrance is pted. Radiographic criteria for diagnosis of rheumatic rt-disease[10] used in the assessment of cases in this ies have not been generally accepted

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[24] Schiff M. *Arch phys Heilk* 1846 5 667
[25] Curling T B *Med -chir Trans* 1842 25 260
[26] Brown Séquard E *Lancet* 1858 ii 545
[27] Madow L Alpers B J *Arch. Neurol Psychiat* 1954, 72, 440
[28] Brooke Williams R. D *J Pediat* 1954 45 575
[29] Leigh M. D Belton M K Pediatric Anesthesia New York, 1948 p 16
[30] Gerber A. *J Pediat* 1955, 46 67

[1] Green C A *Med Pr* 1941, 103, 523
[2] Gray F G *Amer J Med* 1952, 13 400
[3] Stevenson A C Cheeseman, E A *Ann Eugen*, *Lond.* 19 17 177
[4] Pickles W N *Lancet*, 1943 ii 241
[5] Beers C V *Hereditas, Lund*, 1948, 35, 534
[6] Kaufman O, Scheerer, E *Z ges Anat* 2 *Z Konstl* 1938 21, 687
[7] Perry, C B *Arch Dis Childh* 1940 15 179
[8] Wilson, M. G Schweitzer M *Circulation*, 1954 10, 699
[9] Wilson M G, Schweitzer, M. *J clin Invest* 1937, 16, 555

When both parents have had rheumatic fever the risk their children being susceptible is apparently so great to call for prophylactic chemotherapy throughout the ceptible age period. But in others such prophylaxis still probably justified only when susceptibility has en manifested by the first attack.

## THE CAROTID-SINUS SYNDROME

FAINTING attacks in elderly people are sometimes due increased sensitivity of the carotid sinus The chanism of this increased sensitivity is obscure but seems to be associated usually with atherosclerosis. mours and inflammatory conditions in the neck may o affect the sinus though oddly enough tumours of e carotid body do not The syncopal seizure which y be precipitated by some quick movement of the ad, by bending or by lifting a heavy weight, is often eded by a brief aura consisting of tinnitus blurred ion, hallucinations, dizziness or acroparaesthesiæ It followed by a short period of unconsciousness during ich pallor sweating and convulsions may be observed agnosis depends on reproducing the aura by light essure or massage over the carotid sinus heavy pres re is dangerous in patients with sensitive sinuses. Even th light massage the patient may faint but fainting n usually be averted by releasing the pressure as soon symptoms are manifest Sensitivity is usually con ned to one sinus, but may occasionally be bilateral

Conservative treatment includes advice to avoid tight llars sudden head movements bending lifting or uatting down. Drugs known to increase carotid sinus nsitivity should not be given these include digitalis orphine ephedrine nitrites methacholine and thyroid tract The belladonna alkaloids on the other hand crease sensitivity and these may be administered gether with a sedative In intractable cases surgical nervation of the sinus[11] is often successful but irradia on is simpler and very nearly as effective Greeley t al.[12] apply 200-220 kV with a 2 mm filter of copper d a 1 mm. filter of aluminium a 50 cm target-skin distance 200r (measured in air) and a 5 cm square portal Two or three treatments are given preferably on alternate days The total dose to the area of the affected sinus is 500r if the condition is unilateral and 400r if it is bilateral Stevenson[13] used much the same dosage which seems to be quite free from risk. By this means Greeley and his colleagues have completely relieved some 60% of their patients and have failed to improve only some 5% The relief is prompt and in most cases lasts several years.

## RESISTANCE TO INSECTICIDES

THE success of synthetic insecticides in preventing insect borne disease has been jeopardised by the emergence of insecticide resistant strains In September, 1953 the World Health Organisation called a conference in Rome to assess the problem and consider future policy, and the proceedings have now been published[14]

The position was summarised by S W Simmons of the U S Communicable Diseases Center in these words

> In this document we list 35 species of insects of public health importance which have been reported to be resistant Among these 26 species have been confirmed on the basis of experimentation and only 19 are proved disease vectors of importance In view of the thousands of tons of D.D.T and related insecticides which have been used in the past several years this record of resistance while disappointing should not be considered catastrophic

These are curious statements for if indeed nineteen important disease vectors have become resistant this is surely worse than disappointing but his assertion does not seem to have been established We can trace published information on physiological insecticide resistance only in strains of the following insects: (1) the housefly (including *Musca domestica vicina*) (2) members of the *Culex pipiens* complex (*C fatigans* (?) *C autogenicus*) (3) salt marsh culicines in various parts of North America (including *Aedes sollicitans A tæniorhynchus A dorsalis A nigromaculis* and *Culex tarsalis*) (4) the body louse and (5) the German cockroach In addition quantitative field data strongly indicate resistance in *Anopheles sacharovi* and probably the ordinary bed bug Even if the definite instances of resistance number no more than a dozen (including four disease vectors) the matter is serious enough

The term resistance covers several quite different things The normal high resistance characteristic of some species is obviously different from resistance in a strain of a susceptible species Resistant strains usually result from the selective action of widely used insecticide True physiological resistance implies the capacity to survive large doses of a particular poison This may be due to various causes reduced permeability of the cuticle detoxication mechanisms or other unknown factors Tolerance to dicophane (D D T) in houseflies for example may be due to at least three kinds of resistance Physiological resistance may be slight (say twice to ten times normal) or great (several hundred times normal) Only where it is great (for example the resistance of strains of flies to chlorinated hydrocarbons) is insecticidal control definitely excluded; slight resistance does not necessarily lead to high resistance and may sometimes be offset by increasing dosage It seems probable that the capacity to develop resistance varies widely between different species and in relation to different insecticides

Selective mortality due to insecticide sometimes leads to the emergence of a race hypersensitive to the insecticide which survives by avoiding the insecticide (e g *Anopheles albimanus* in Panama) Moreover when a mosquito has both domestic and ' wild ' strains

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Wilson, M G., Epstein N Helper H N Hain K *Circulation* 1953, 8, 879

Cattell, R. B Welch, M L. *Surgery* 1947 22 59

Greeley H P., Smedal M I Most W *New Engl. J Med* 1955 252 91

[13] Stevenson C A *Radiology* 1948 50 207

[14] First International Conference on the Control of Insect Vectors of Disease Rome Oxford Blackwell Scientific Publications 1954 Pp 396 5 s. 6d

(the former frequenting houses and the latter living away from man) insecticide will selectively destroy the "domestic" strain, while larvæ of the "wild" types remain plentiful in the breeding foci This situation has been suspected in regard to *A gambiæ* in Mauritius and *A labranchiæ* in Sicily

Field workers have had little success in countering resistance by changing to different insecticides or in other ways The Rome conference showed that the problem is being keenly studied.

## VACCINE LYMPH AND AUREOMYCIN

THE annual report of the Institute for Medical Research of Malaya[1] describes the financial saving effected by salvaging contaminated batches of vaccine lymph About a third of the vaccine lymph prepared had been rejected because it was contaminated with gas-forming anaerobic organisms It was found that when 1 g of aureomycin was added to each litre of lymph, the sterility tests laid down by the Therapeutic Substances Act could be complied with Thus expenditure of $26 on aureomycin resulted in the saving of $24,000—the value of six batches of vaccine lymph contaminated with gas-forming anaerobes, which formerly would have been discarded

This procedure may not be wholly devoid of danger Although the addition of antibiotic enabled the official sterility requirements to be complied with, any toxin formed by the bacteria might remain, and in the sterility tests the antibiotic might obscure the presence of micro-organisms which might remain alive and multiply when the lymph was used for vaccination Many years ago in Australia economies effected by supplying diphtheria prophylactic in large containers were followed by infection and death of children who received infected prophylactic, and the economy was promptly abandoned

## HYPOTHERMIA IN THE PREMATURE

PREMATURE infants tend to have a lower body temperature than full term infants, and, broadly speaking, the degree of hypothermia varies directly with the degree of prematurity This hypothermia is mainly due to *immaturity of the physical mechanisms of heat* regulation, such as shivering, vasoconstriction and vasodilatation of the skin vessels, and sweating, but premature infants have the additional disadvantages of a relatively large surface area per unit of weight, slight muscular activity, and poor insulation with subcutaneous fat, all of which militate against maintenance of body-temperature Day[2] has shown that the reaction to these unfavourable influences includes increase in the basal metabolic rate and in heat production, but there is evidence that low temperatures are better tolerated by premature than by full-term infants Grossly premature infants with a birth-weight of 2–3 lb usually have a fairly constant temperature of 93–96°F for two or three weeks, thereafter the temperature rises, in the course of a few days, to 97–98°F, which is normal for full term newborn infants The care of premature infants has long included attempts to raise the temperature to the level found in mature infants, but such measures have had little success

For some years a few experienced pædiatricians, including Clement Smith,[3] have been satisfied with a temperature of 93–96°F in the first two weeks of life in grossly premature infants, and the wisdom of this view is now being widely recognised Tobler,[4] Debre,[5] and others assert that it is unnecessary, and even harmful, artificially to increase the metabolic rate and thus the oxygen requirements of these feeble infants, the vasodilatation induced by excessive heat, cause a shock with consequent deterioration and de Joppich and Schäfer[6] state that undue warming c stitutes a greater danger than hypothermia In a se of 48 premature infants they withheld artifical he unless the temperature fell below 90°F They found th infants of all degrees of prematurity down to $2^1/_4$ birth weight maintained approximately the temperat found on admission to hospital In infants weigh $2^1/_4$–$4^1/_2$ lb at birth the temperature rose to about 9 in the fourth week The amount of food taken and weight course were much the same as in those tre by artificial heat, but the rate of respiration was a li less, as would be expected with a lower metabolic r All those with a birth-weight of $4^1/_2$–$5^1/_2$ lb attaine temperature of 97–98 4°F within two to four days.

Experience with artificial hypothermia in anæsth has increased our knowledge of the response to abnor low temperatures, and this knowledge has been app to premature infants[7] Experience so far with ind hypothermia will do little to shake the belief of clini that premature infants with exceptionally low temp tures have a poor prognosis Apparently it is u and possibly dangerous to take vigorous measure raise the temperature of premature infants, but t should be safeguarded from chilling, especially in first twenty four hours of life when pronounced hy thermia is more harmful than it is later A uni atmospheric temperature of about 75°F, without adju such as hot water bottles, is probably all the hea that is necessary Good nursing, attention to fee technique, and prevention of infections are more li to increase the survival-rate of premature infants t concentration on raising the body temperature

## BRITISH JOURNAL OF HÆMATOLOGY

SPECIALIST journals in hæmatology have a respect history *Folia Hæmatologica* did not survive the war, but *Le Sang*, published in Paris, has been appea regularly for many years, *Blood*, published in the U.S started its 10th year with the January issue, Switzer produces *Acta Hæmatologica*, and there are one two other European publications The British sc of hæmatology, though active, has hitherto had journal of its own workers have published their find in general journals or in specialist journals dev to clinical medicine, clinical pathology, or pure patho The *British Journal of Hæmatology*, a new quart of which the first issue has now appeared,[8] meets a need, justifying its addition to the already overlo journal racks

The first issue ranges widely the subjects incl management of acute leukæmia, hæmophilic blo yet another Rh antigen, and erythropoiesis in irradiated rat The pages are of good paper, and illustrations are clear References include the title the articles The editorial board declares that "o papers closely related to the author's work should referred to, exhaustive lists should be avoided"

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DR ALBERT SCHWEITZER, the French philosoph musician, and medical missionary, has been appoint an honorary member of the Order of Merit.

MR RICHARD FORT, M P, has been appointed to th Medical Research Council in the vacancy created by th retirement of Mr Richard Wood, M P

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[1] Annual Report of the Institute for Medical Research of the Federation of Malaya 1953 Kuala Lumpur Pp 104 5s 10d

[2] Day R *Amer J Dis Child* 1943 65 376

[3] Smith C A Physiology of the Newborn Infant Oxford 1951

[4] *In* Moderne Probleme der Pädiatrie Basle, 1954, p 55

[5] *Sem Hôp Paris*, 1953, 29 2462

[6] Joppich von G, Schäfer H *Dtsch med Wschr* 1955, 80 1

[7] Lacomme, M Laborit H, Chalrun J Boreau, T, David,
*Bull Féd Soc Gynec Obstet* 1952, 4, 643

[8] *British Journal of Hæmatology*, vol I no 1 January 19 Editor Dr J V Dacie Postgraduate Medical School Duc Road London, W 12 Published by Blackwell Scient Publications 24, Broad Street, Oxford 30s per annu 15s per issue

# Social and Biological Factors in Infant Mortality *

## IV THE INDEPENDENT EFFECTS OF OCIAL CLASS, REGION, THE MOTHER'S AGE AND HER PARITY

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the third paper of this series[3] it was shown that the rences between the social classes in their stillbirth infant mortality rates are altered very little by ing for class differences in the ages and parities of mothers. A measure of independence between the on of the three factors—the mother's age her parity her social class—on the stillbirth and infant mortality is thus suggested The present paper shows that e is in fact a considerable degree of independence defined sense and goes further by showing that e is a regional factor—based on the part of the ntry in which the parents lived at the time of the h—which is related to the mortality rates and has action which is independent of the other three ors.

he sense in which the word independent ' is used in context is best illustrated by considering the relation discussed in the second paper of this series[2] between ernal age and parity and the stillbirth rate It was n there that at any given parity † the stillbirth increases as the mother s age increases This pattern emphasised was evident for every parity considered to the ninth Conversely in mothers of a given age p the rate is high for first births, *falls for second* third births and rises again for later births until rate for first births is approached in very late preg cies. This is true of every age group In the sense d here the mother s age and parity are regarded as dependent influences on the stillbirth rate Each or has its characteristic effect whatever the value he other may be: the effect of either cannot be plained away by the other This does not mean t the effect of age, for instance is exactly the same each parity—the stillbirth rate appears to begin its l rise at an earlier age in first births for example— the general pattern is unaffected The factors selves are, of course always associated in indi als; parity and age obviously increase together— hers of four children will, on the average be older n mothers of one child But from the point of view stillbirth youth (except possibly extreme youth) is advantage for mothers of four children as it is for thers bearing their first child

### Results

In this paper the first step is to show that mother's e and *parity* each independent of the other have ir effects in the different *social classes* conversely at the social-class factor acts in the same way at different ages and parities Age, parity, and social class are thus shown to be independent in the sense in which that term is used here

Secondly similar relationships are shown between *region* (or part of the country) and mother s age and parity demonstrating the independence of these three variables

As a third step, *social class* and *region* are shown to be independent of one another

Since these independent' relationships apply to all three mortality rates (stillbirth neonatal, and post neonatal) a different rate has been used to illustrate each step though each is documented in the relevant table for all three rates The post neonatal rate is chosen to illustrate the first step the neonatal the second and the stillbirth rate the last

### *The Independent Action of Social Class and Mother s Age and Parity*

Fig 1 shows the variation of the post neonatal mortality rate with social class the mother s age and the mother s parity It is based (as are all the tables and figures in this paper) on the single legitimate births which occurred in England and Wales in 1949 For clarity the mothers have been grouped into three broad age categories and into three categories according to their parity making nine categories of age and parity The usual five social classes have also been grouped into three by amalgamating class I with class II and class IV with class V These amalgamations in terms of age parity and social class were made to bring out the main features of the known variation of the rates (for instance the fact that the stillbirth rate for mothers of a given age is high for first births falls for second and third births and rises again for later births) They do not conceal any irregularities which affect the arguments that follow They were needed also to give reasonably large numbers in each category of the various tables—always with the exception that mothers under 25 having their fourth or

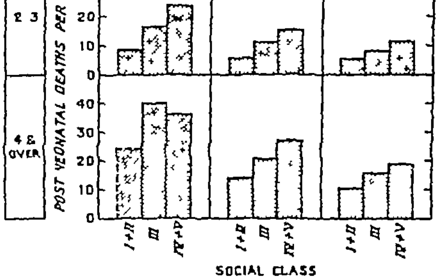

Fig 1—Variation in post-neonatal mortality-rates according to the social class of the father and the mother's age and parity

Single legitimate births in England and Wales, 1949 The lightly shaded column indicates a rate based on fewer than 10 deaths

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* eries of articles reporting an inquiry made jointly by the Social Medicine Research Unit (Medical Research Council) and the General Register Office The articles[1–3] were prepared by the Unit in collaboration with the General Register Office and have been approved for publication by the joint working party responsible for the inquiry

† The parity of the mother is defined here as the number of children she has borne—surviving dead or stillborn—including the present one

TABLE I—VARIATION IN STILLBIRTH AND INFANT MORTALITY RATES ACCORDING TO THE SOCIAL CLASS OF THE FATHER, AND THE MOTHER'S AGE AND PARITY

(Single, legitimate births in England and Wales, 1949)

| Mother's parity (no of children) | Social class | Stillbirths * | | | Neonatal deaths † (at ages under 4 weeks) | | | Post neonatal deaths † (at ages 4 weeks–1 year) | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Mother's age | | | Mother's age | | | Mother's age | | |
| | | Under 25 | 25–29 | 30 and over | Under 25 | 25–29 | 30 and over | Under 25 | 25–29 | 30 and over |
| 1 | I and II | 16 2 | 19 5 | 35 5 | 12 3 | 14 5 | 21 0 | 4 6 | 4 2 | 4 4 |
| | III | 17 4 | 23 9 | 40 3 | 15 8 | 16 8 | 24 0 | 9 7 | 5 7 | 6 9 |
| | IV and V | 18 9 | 27 5 | 47 1 | 18 7 | 17 9 | 28 6 | 12 7 | 10 3 | 10 4 |
| 2 3 | I and II | 10 8 | 10 2 | 18 3 | 14 0 | 10 5 | 12 0 | 8 6 | 5 8 | 5 7 |
| | III | 12 9 | 13 6 | 21 2 | 15 7 | 12 8 | 15 0 | 16 6 | 11 1 | 8 1 |
| | IV and V | 12 7 | 16 7 | 25 8 | 18 9 | 14 5 | 17 3 | 23 7 | 15 1 | 11 2 |
| 4 and over | I and II | (23 6) | 15 4 | 20 2 | (32 3) | 12 8 | 18 3 | (24 2) | 14 2 | 10 6 |
| | III | 17 9 | 18 8 | 34 1 | 29 4 | 16 3 | 18 1 | 30 9 | 20 7 | 15 6 |
| | IV and V | 14 7 | 19 1 | 37 6 | 24 4 | 17 0 | 22 7 | 36 2 | 27 0 | 18 7 |

* Per 1000 live and still births
† Per 1000 live births
Rates in parentheses are concerned with fewer than 10 deaths (or stillbirths)
Births for which social class or the mother's age, or parity, were not stated are excluded from the table

later child are unusual anywhere, and in any class (they constitute 0 4% of the total births) Most of the rates are concerned with substantial numbers of deaths, but those calculated from fewer than ten are indicated in the tables and figures Space forbids a detailed statement of the numbers of births involved, but, apart from the small category just mentioned, all rates are based on more than 1000 births

It can be seen in fig 1 that, with the single exception of this small category, the well-known rise in the post-neonatal mortality rate from social classes I and II to social classes IV and V occurs within each of the nine categories

From the other point of view—whether age and parity act independently within each class group—the same figure shows that the characteristic rise in th neonatal mortality rate with increasing numbe children, and the high rate among children of yo mothers,[2] is present within each of the three large so categories used For instance the rate for classes IV V (the group with the highest rate) can be seen to incre with parity in each category of mother's age (readi down the columns in fig 1), and to decline with increa maternal age in each parity, though less markedly first births (reading across from left to right) T characteristic pattern appears also in social classes I II and in class III Thus essentially the same patte variation with age and parity which prevails fo whole country is present in each of the three groups

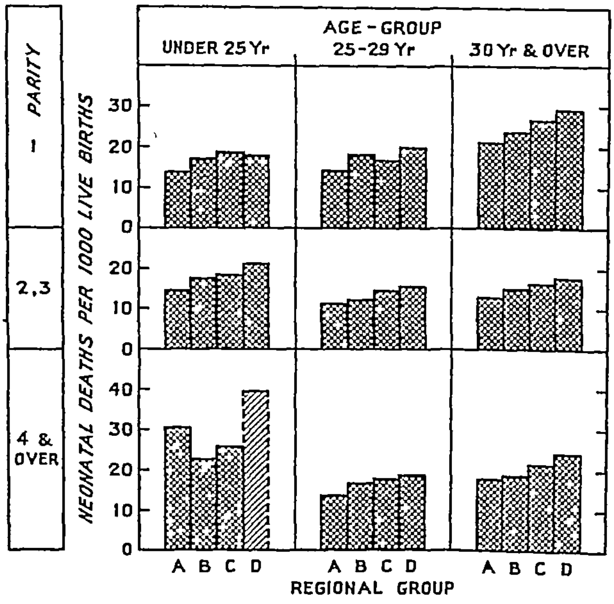


Fig 2—Variation in neonatal mortality-rates according to the part of the country in which the parents lived at the time of the birth and the mother's age and parity

Single, legitimate births in England and Wales, 1949 The lightly shaded column indicates a rate based on fewer than 10

It may therefore be said that social class influe the post neonatal mortality-rate in the same way, whatever the mother's age or parity, and that age and parity affect the rate in much the same way in the different social classes Table I shows that this is true also for still births and neonatal deaths Age, parity, and social class are therefore three factors, the action of each of which on stillbirth and infant-mortality rates can be said to independent of the action of the other two

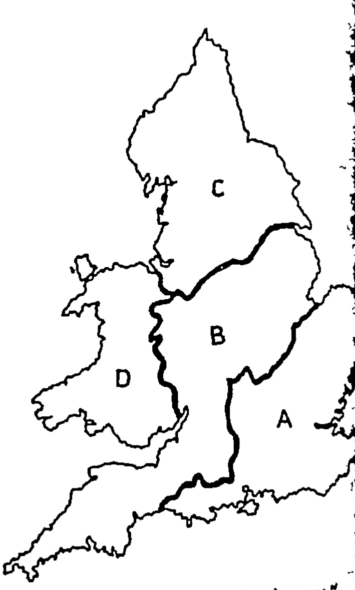


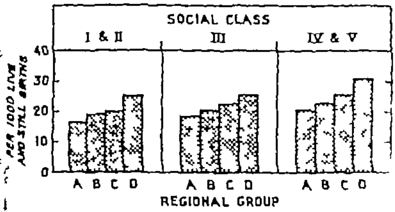
Fig 3—The four "regional groups."

*The Independent Action of Region and Mother's Ag*
*Parity*

Fig 2 shows, for mothers of different ages and par how the neonatal mortality rate varies according to part of the country in which the parents lived at time of the birth As before, nine categories of mot age and parity are used The ten "standard regions the country are arranged into four broad regional gr as shown in fig 3 Each regional group consists regions whose stillbirth and infant mortality rates similar The neonatal mortality rates in 1949 for three regions in group A (the South East of Engla for instance, were all less than those for the three reg in group B, and so on Wales showed the worst ra This order held for stillbirths also, but the order the post-neonatal mortality rate was A, B, D, C Northern group, C, that is, had the worst rate (in wh the well-known excess of mortality from respirat infections in young children in the North-East, natur played a part)[5]

It will be seen that the order A, B, C, D of the neonat mortality rate is repeated through fig 2 There is doubt about the general trend though there are m exceptions, and once more there is no partic pattern in the special group of mothers under 25 four or more children

Conversely, and again with only minor exceptions, pattern of variation of the neonatal mortality rate w the mother's age and parity which prevails for the wh country can be seen in each regional group In all



—Variation in the stillbirth-rate according to the social class of the her and the part of the country in which the parents lived at the e of the birth.

ingle, legitimate births in England and Wales 1949

s of the country, neonatal mortality shows U-shaped erns Birth rank for birth rank children of young hers and of "old" mothers have relatively high rates larly first children and fourth or later children tend how high mortality rates There is however a ption first children of young mothers do in fact e low rates. Very interestingly in terms of the nt thesis table II shows that this exception is itself ated in each of the four regional groups

he part of the country in which the parents live when child is born appears therefore, to influence the atal mortality rate in much the same way whatever mother's age or parity and conversely these ogical factors have a similar effect in different parts he country

able II shows that the same generalisations hold true the stillbirth and post-neonatal mortality rates Age ity and region as studied are again a trio of factors e action on the stillbirth and infant mortality rates s to be largely independent

### *Independent Action of Social Class and Region*

g 4 shows the variation of the stillbirth rate with al class and region the five social classes being arranged in three groups as before It is clear that the established regional pattern of an increase from group A to group D is reproduced in each class Wales for instance had consistently the worst record Furthermore the rise in the mortality with descent in the social scale from classes I and II to classes IV and V, is seen in the four groups individually

A glance at table III shows also that class and region are similarly independent in their actions on the neonatal and post neonatal mortality rates except that post-neonatal rates for the regional groups are not always in the expected order, with the North showing up worst. The two factors of region and social class can therefore be regarded as independent influences on the stillbirth and infant mortality rates

E II—VARIATION IN STILLBIRTH AND INFANT MORTALITY ATES ACCORDING TO THE PART OF THE COUNTRY IN HICH THE PARENTS LIVED AT THE TIME OF THE BIRTH ND THE MOTHER'S AGE AND PARITY

(Single legitimate births in England and Wales 1949)

| her's ity o. of ldren) | Regional group ‡ | Stillbirths* | | | Neonatal deaths † (at ages under 4 weeks) | | | Post neonatal deaths † (at ages 4 weeks–1 year) | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Mother's age | | | Mother's age | | | Mother's age | | |
| | | Under 25 | 25–29 | 30 and over | Under 25 | 25–29 | 30 and over | Under 25 | 25–29 | 30 and over |
| 1 | A | 15·4 | 20·4 | 30·3 | 13·7 | 14·5 | 21·4 | 7·0 | 5·3 | 4·6 |
| | B | 17·5 | 21·1 | 42·4 | 17·0 | 18·2 | 23·8 | 9·[illegible] | 5·8 | 6·4 |
| | C | 18·7 | 26·1 | 41·8 | 18·3 | 16·9 | 27·1 | 13·3 | 7·8 | 9·0 |
| | D | 24·4 | 32·8 | 52·1 | 17·8 | 19·8 | 20·6 | 12·0 | 6·6 | 4·9 |
| 3 | A | 10·6 | 11·8 | 10·2 | 14·3 | 11·1 | 13·0 | 12·0 | 7·5 | 5·7 |
| | B | 13·1 | 14·0 | 20·9 | 17·1 | 12·1 | 15·0 | 17·9 | 10·4 | 7·9 |
| | C | 13·0 | 15·6 | 23·8 | 17·8 | 11·6 | 16·[illegible] | 21·1 | 15·4 | 11·2 |
| | D | 16·2 | 15·3 | 26·8 | 20·8 | 15·0 | 17·[illegible] | 24·8 | 15·2 | 8·8 |
| 4 and more | A | 16·0 | 16·9 | 31·5 | 30·4 | 13·5 | 18·0 | 23·4 | 13·0 | 10·3 |
| | B | 14·[illegible] | 17·2 | 33·7 | 22 | 10·7 | 18·8 | 31·7 | 12·[illegible] | 10·0 |
| | C | 20·0 | 20·3 | 37·0 | 25·8 | 1[illegible]·8 | 21·1 | 49·4 | 31·4 | 19·5 |
| | D | (19·2) | 23·0 | 38 | (39·2) | 15·0 | 24·1 | 33·8 | 22·7 | 21·1 |

r 1000 live and still births
r 1000 live births
Rates in parentheses are concerned with fewer than 10 deaths (or stillbirths).
Births for which the mother's age or parity were not stated excluded from the table
Regional groups consist of the following standard regions
A—Southern Eastern and London and South East
B—South Western, Midland and North Midland
C—Northern, North Western and East and West Ridings
D—Wales

### 'Vulnerable Groups'

In the second paper of the present series, three "vulnerable groups" with particularly high mortality rates were identified, in terms of the biological factors of mother's age and parity These groups were (i) mothers aged 35 or over having their first babies (ii) mothers aged 40 or over of any parity and (iii) young mothers with large families for their age (under 20 with two or more children under 25 with three or more) The first two groups have high rates of stillbirth, children of mothers in the third group have high post neonatal mortality rates Table IV shows that these groups have an unfavourable experience in all classes and regions considered It is interesting thus in the light of the foregoing discussion that the social-class factor operates independently even at the high levels of mortality set by the biological disadvantages there being a clear trend in the death rates from classes I and II to IV and V The regional factor also is seen to be effective at these levels with the North (C) once again showing up badly in the post neonatal period

TABLE III—VARIATION OF STILLBIRTH AND INFANT MORTALITY RATES ACCORDING TO THE SOCIAL CLASS OF THE FATHER, AND THE PART OF THE COUNTRY IN WHICH THE PARENTS LIVED AT THE TIME OF THE BIRTH

(Single legitimate births in England and Wales, 1949)

| Regional group ‡ | Stillbirths* | | | Neonatal deaths† (at ages under 4 weeks) | | | Post neonatal deaths † (at ages 4 weeks–1 year) | | |
|---|---|---|---|---|---|---|---|---|---|
| | Social class | | | Social class | | | Social class | | |
| | I and II | III | IV and V | I and II | III | IV and V | I and II | III | IV and V |
| A | 18·0 | 18·9 | 20·7 | 12·0 | 14·4 | 15·5 | 5·0 | 7·3 | 9·7 |
| B | 19·8 | 21·0 | 23·3 | 14·0 | 16·0 | 18·9 | 5·6 | 10·8 | 14·1 |
| C | 20·4 | 22·8 | 25·0 | 14·2 | 17·1 | 20·9 | 6·0 | 13·6 | 20·8 |
| D | 25·[illegible] | 25·6 | 30·8 | 15·0 | 19·7 | 21·0 | [illegible]1 | 13·0 | 18·0 |

* Per 1000 live and still birth
† Per 1000 live births
‡ For definitions of regional groups see table II
Births for which social class was not stated are excluded from the table.

### Comment

Strictly speaking it has not been demonstrated that any one of the four factors exerts its characteristic effect when *all* the other three are held constant If the factors are thought of as 1 2 3 and 4 factor 1 (mother's age for instance) has been shown to exert its influence when 2 (mother's parity) and 3 (social class) are held constant but it has not been shown that it does so when 2 3 and 4 are *all* held constant This is for lack of the necessary data—a lack which will be remedied in the analysis for 1950 It is felt however that enough has been shown to make it highly likely that the action of each of the four is largely independent of the action of the other three

As mentioned earlier this independence must not be confused with the fact that these influences on the

Dr. Robert Hellg Library

TABLE IV—"VULNERABLE GROUPS" THE VARIATION OF THE STILLBIRTH AND INFANT MORTALITY RATES WITH THE SOCIAL CLASS OF THE FATHER, AND THE PART OF THE COUNTRY IN WHICH THE PARENTS LIVED AT THE TIME OF THE BIRTH, IN THREE "VULNERABLE GROUPS"

(Single, legitimate births in England and Wales, 1949)

| Social class and regional group | Stillbirths * | | | Post neonatal deaths † | |
|---|---|---|---|---|---|
| | In primi paræ aged over 35 | In all mothers aged over 40 | In mothers of all ages and parities | In young mothers with large families for their age ‡ | In mothers of all ages and parities |
| Social classes | | | | | |
| I and II | 45 5 | 42 7 | 19 0 | 13 6 | 5 8 |
| III | 49 2 | 48 8 | 21 1 | 25 8 | 10 6 |
| IV and V | 54 2 | 53 1 | 23 9 | 34 3 | 15 6 |
| Regional groups § | | | | | |
| A | 43 5 | 45 6 | 18 9 | 18 4 | 7 4 |
| B | 51 7 | 47 4 | 21 4 | 24 9 | 10 9 |
| C | 63 3 | 52 7 | 23 4 | 39 7 | 15 0 |
| D | 60 4 | 55 3 | 27 0 | 36 8 | 14 0 |

* Per 1000 live and still births
† Per 1000 live births
‡ Defined here as those aged 16–19 having second or later births, and those aged 20–24 having third or later births
§ For definitions of regional groups see table II

mortality-rates are always associated in the same individual The "standardisation" discussed in the preceding paper[3] deals with the fact that, for instance, "old" age at childbirth, low parity, and social class I are often associated in the same individual—that is, in statistical terms, there is a correlation between these attributes in individuals The present paper shows more fully that age, parity, and social class make their separate contributions to the mortality-rates—that is, their "action" is independent in spite of this correlation As was stressed in an earlier paper,[2] the differences in the effects of maternal age and parity on stillbirths, compared with their effect on deaths from infection in the post neonatal period, for instance, are related to the well-known differences in the immediate causes of death at these periods Though age and parity may be considered "biological" factors, their action in the post neonatal period is probably through what may be called "social" ætiology—increased opportunity for infection in large (and maybe overcrowded) families, the economic consequences of having a large number of children, the difficulties of the young mother in coping with a large family, and so on[1 2 4 7 8]

The fact that class, age, and parity are independent factors means more than that class differences cannot be accounted for in terms of the mother's age and parity The converse is also true we cannot account for the variation of mortality rates with age and parity in terms of class differences In particular we cannot explain away the decrease of the post neonatal mortality rate with the increasing mother's age, and its increase with higher parity, by saying that young mothers with large families are commonest amongst social classes IV and V, and that it is therefore to be expected that children of such mothers should have a high death rate The trend of the post neonatal rate with maternal age and parity is apparent in social classes I and II, and in III, as well as in IV and V

The presence of a geographical trend which cannot be explained away either by saying that there are relatively more mothers in social classes IV and V in the North (and in Wales), or that they have larger families there, is also interesting—especially in so small and (compared with many others) so homogeneous a country as our own There have been many studies of regional differences in infant mortality,[5 6] and we know that these high mortality rates in the North and in Wales have been present for a long time Social class comparisons between regio difficult The occupations of the fathers in the differ regions may be so different that comparison of classes may be invalidated Social class IV in E Anglia, for instance, will include many agricult workers whose wives and children have low stillbirth infant-mortality rates, the same class in Durham include many miners with high-rates However, so classes I and II probably mean much the same in diffe parts of the country It is interesting, therefore, not only do social classes I and II in Wales regist higher stillbirth-rate (25 2 in 1949) than classes I a elsewhere, but they register a higher rate than clas South East England (21 4) In any event, the inde dence demonstrated is sufficient to encourage fu inquiry along at least two lines other than those considered—namely, (1) the effects of climate, and local and administrative differences in the applicat medical knowledge

The independence which is discussed here for all factors is, of course, by no means absolute There room for considerable "interaction" in the sense of effects of two factors reinforcing or opposing each o and, no doubt, statistical tests will show that such actions are "significant"—*that is, they are not lik* be mere chance effects One example of this, ment later, but not discussed at the time for the sake of c is that the effects of age and parity on the neo mortality rate cannot be regarded as strictly indepe even within the broad definition used in this paper children of mothers over 25 years of age have a high compared with second and third children of such mot but this is not true for mothers under 25 This, how as already explained, does not affect the independ of action of the pair of factors, age and parity, in different classes and regions Again, it may well be that social class differences are greater in certain cir stances than in others The stillbirth rate seems sensitive to class differences amongst young mot having their second and third babies than amongst mothers in the same situation (table I ) Possibly effects of age and parity, though similar in direction, different in degree at different social levels, or in diff parts of the country However, such effects are more subtle (and some of them require larger num to show with certainty) than the degree of independ which has been demonstrated, and they do not ex away the characteristic action of the separate fact

From the point of view of further reduction of which are at a very low level and (except possibly stillbirth rate) are still falling, the present finding forms with the view that, in modern England and W at any rate, further progress may still be possible several lines A combination of physiological and s logical research may tell us how and why mother's and parity have their different effects on infant deat different ages, social, administrative, and clim research has much yet to explain of the social geographical differentials

## Summary

Four factors—the mother's age and parity, her soc class, and the region (or part of the country) in which t parents lived—are shown to exert largely "independent influences on the stillbirth, neonatal, and post neonat mortality rates amongst single, legitimate births England and Wales in 1949 The word "independent" used in a defined sense—each factor exerts its own chara teristic effect whatever the values of the other facto

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*References at foot of next column*

# Special Articles

## YOUNG PEOPLE

ost children do not get into the hands of the police the proportion who pass through a phase of delin ncy is far greater than official figures suggest Two books dealing with adolescents—Pearl Jephcott's e *Young People*[1] and John Barron Mays's *Growing in the City*[2]—consider the influences to which young ple are nowadays exposed including the somewhat t impact of our youth services

### EIGHTY BOYS

r Mays, warden of the Liverpool University Settle t, gives the results of a study he began in 1950 venile delinquency in the tightly packed heart of crowded seaport As a social worker he was at startled to find that some of the most active friendly coöperative of his club boys had been in court or on ation and he set about gaining the confidence of these boys only, but of others who had never been rehended in order to find out how common among n were breaches of the peace and what attitude they lves had to such adventures He found that of the oys included in the study a very large proportion had n part, at some time during childhood or adolescence legal practices—'lorry-skipping' petty pilfering and o-lifting for the most part though breaking entering thieving were not at all uncommon The peak age uch delinquent behaviour was 13 by 14 most he boys were beginning to grow out of it. Those who me adult criminals were very few and were he d, usually emotionally insecure and often of less n average intelligence Indeed he finds it useful to nguish between delinquents and criminals ugh he thinks the two types overlap):

> Where severe emotional disorder is allied to an environ t which prompts illegal activity the child will develop the criminal and where the degree of emotional urbance is very slight and the environment is particularly ducive to illegal behaviour the child will more likely me the delinquent.

s an environment conducive to illegal behaviour the kides of Liverpool must rank high He describes its y worlds—the passionately Roman Catholic Irish ulation the indigenous Protestants nowadays more d in their faith and hence more tolerant than formerly processions on St Patrick's day (though still apt to brate Orange day with a counter-demonstration) coloured population the dubious clubs and the bels the drug traffic and the cramped and cramping eation of the tenements and mean alleys. The city sing committee are steadily demolishing unsafe anitary property and rehousing families, either in new ung estates on the outskirts of the city or in new cks of flats but promising as this sounds, they are ys thinks, laying up fresh trouble for the future So cious is land that the blocks going up are large and high and provisions in or round them for communal activities have been deliberately ruled out Playgrounds of course, are exceedingly few and though all the boys of the neighbourhood are madly keen on football and often get up teams in their own streets, they have to practise in the streets themselves and inter-street matches have to be played on waste land, on bombed sites or in car parks

The growing boys are thus cooped in narrow surroundings which give them no scope for adventure and little for violent physical exertion At 11 12 and 13 they are at the height of that gregarious phase of development when the mood and opinion of contemporaries seems the only reality worthy of attention It is the age for gang life and gangs as Mays points out, need not necessarily engage in nefarious activities a street football team is one form of gang activity and such teams are often well organised by the boys themselves

Nevertheless of the 80 boys interviewed 30 had been convicted on one or more occasions and 4 were convicted after the interview They had collectively been guilty of larceny, breaking and entering wilful damage to property receiving stolen goods and railway offences A further 22 boys admitted to delinquencies for which they had never been brought into court. It is hard in these circumstances to believe that the remaining 24 had perfectly clean hands, and indeed 11 of them admitted to lorry skipping—which generally means in their society tasting the cargo of fruit nuts, or sugar which such lorries are bringing up from the docks and perhaps pilfering some for sale later If these 13 are added the confessed delinquents in this group of 80 total 69 and the remaining 11 are more likely to have been reticent than entirely law abiding

Their leisure interests were singularly stereotyped football was the usual Saturday afternoon activity, followed by a visit to the pictures on Sundays they lay abed till noon, played football after dinner, and in the evening got up a game of darts or went to the cinema again They lived in fact very boring lives and delinquents it has been *observed* are *above the average* in their zest for exciting recreation and dangerous play

Taking part in criminal acts, as one boy put it made you 'sweat,' but this very sensation of almost physical excitement was a source of pleasure and therefore an incentive in its own right Adventure and freedom another lad said were what he and his friends wanted most Daring physical feats enable a boy to prove himself to himself as well as to his friends in most normal children Mays says there seems to be a real need to experience express and thereby master fear' Well for us that it should be so it is an urge which won for us the Battle of Britain No lawful activity open to these boys provided risk and excitement of the degree they needed. They had not even enough playing space to work off their abundant physical energy Moreover they live in a society which looks leniently on delinquency they do not fall into great disgrace for committing minor crimes and if they are caught in a major crime their parents and associates are more likely to think them unlucky than wicked It is interesting that religious teaching seems to have had little effect on their behaviour About half of the 80 were strict Roman Catholics and the other half though labelled Protestants had on the whole little to do with religion once they had given up Sunday school The code of their neighbours in fact outweighed the precepts of the Churches and religion even among those who practised it was a thing apart from everyday affairs and not a way of life

Most of them as they matured came to conform to the minimum demands of the law, and one sign of this maturation was that they began to realise the consequences of their actions to those they injured to themselves and to their parents and family Those who

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[1] London Allen & Unwin 1954 Pp 168 12s. 6d.
[2] Liverpool University Press 1954 Pp 216 1[illegible]s 6d

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### DR. HEADY AND OTHERS REFERENCES

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were seriously emotionally disturbed, however, seemed incapable of this normal maturation they needed more extensive treatment than punishment or disapproval, and for want of it became trapped in a criminal pattern

The part the youth services played in the lives of these boys was evidently not great, or at all events not crucial in altering their behaviour The hard-working youth leaders, using poor, ill equipped, and unattractive rooms and drill halls, have all they can do to keep their clubs going and the boys interested The possible span of club life is four years, and the 80 boys interviewed had on an average belonged for two There is seldom any link between the club and the family, and seldom much family encouragement to a boy to belong to a club

### *THE CLUBS*

These 80 boys had actually belonged to clubs, however Miss Jephcott and her research team, in trying to find out what proportion of boys and girls actually join clubs, interviewed 939 young people, aged 14–17, living in two districts of central London, one district of Nottingham and four villages—three in Oxfordshire and one in Buckinghamshire Only 1 in 3 of this whole sample of young people belonged to youth organisations In London about 3, and in Nottingham about 2, boys belonged for every girl Those who failed to join included some with a special hobby, some who despised the juvenility of the programmes, some of both sexes who were courting, most of those attending grammar schools, and the more able of the modern school children, as well as the dullards, those with poor health, and those who came from below-average homes

Girls used the clubs less than boys, and for a good reason They were changing rapidly from girls to women, and long before they reached 17 were working and planning for marriage, the next step in a successful career Clubs, offering only the society of contemporary or younger girls and boys, and a programme of games and activities which had no bearing on their main preoccupation, had no possible interest for them They needed opportunities to meet socially young men older than themselves—something which would compare with the "London season" offered to girls of another class There is a good case, as Miss Jephcott mentions, for providing mixed clubs for girls over 16 and older youths—clubs which might arrange tennis and skating parties, cycle runs, dances, picnics, and the like Girls, however, are less often delinquent than boys, and it is hardly likely that clubs of this kind will be regarded as a pressing need just yet Besides, these girls manage to make their own arrangements for meeting youths and marrying them—even though these entail "picking up a fellow at the corner," and doing most of their courting in the cinema

Both Mays and Miss Jephcott agree that the poor standard of decoration and the lack of equipment in many clubs damns them in the eyes of a generation which, rightly or wrongly, prizes the up to date Mays points out another weakness—the common failure of the clubs to make any contact with the family as a whole Both, however, pay great tribute to the work that is done by youth leaders, often under very great difficulties They would be helped, Miss Jephcott thinks, if we would decide whether the business of youth organisations should be primarily to give further education, or to help young people to take part in group relations Should they merely keep children out of mischief, or should they fit him for the adult world ? And should they be adapted to the average child, the under privileged child, or the wild adventurous unmanageable child ? Ethical training, which has always been a concern of youth leaders, now presents new difficulties for it is no longer possible to build on a religious grounding given at home or in church Should the club ignore religion, or attempt a religious programme which may antagonise not only some denominations but some of its members too ? Prob these are not alternatives probably all thing needful If we are to offer them we must have not better, but more, and more varied, youth organisat

### NEEDS

Mays suggests that—in addition to youth lead clergy, school teachers, probation officers, and p should get to know both the child and his home family He writes with keen interest of the sc started about three years ago by the Liverpool p they appointed "juvenile liaison officers" who k touch with children cautioned by the police, intr them to youth clubs and encourage them to atten to know the parents and school-teachers, and talk the children's future with them He would like t these police officers admitted to the classrooms to objectively to the children about crime and good ci ship—about the cost of crime to the community an distress it causes not only to the delinquents but to families He believes, too, that the schools shou taking a leading part in preventing juvenile delinqu by means of parent teacher associations, and by emphasis on character training and social service as he points out repeatedly—what we need above to establish a society with good principles, for a can grow into a habit of good social behaviour as as into a habit of delinquency To do this we may b begin with material things—by giving breathing and community centres to slum populations, and pl space to children Mr Duncan Sandys, Minis Housing and Local Goverment, announced at Birmi recently that the Ministry's aim is "to break the b slums within ten years" This is good news f generation now getting themselves born

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## Public Health

### THE FUTURE OF CHILD-WELFARE CEN

A TIMELY memorandum by the maternity and welfare group of the Society of Medical Officers of sets out "to examine the needs of the mother and of today, to indicate the part played by the child centre in meeting these needs and to conside necessary modification or extension of the trad welfare centre pattern"[1]

In enumerating the aspects of child health to special attention should now be given the grou first place to preventive psychiatry Much of the volume of mental ill health arises from psychic t in the earliest years of childhood, yet treatment o maladjustments and emotional difficulties is delayed until the child reaches school age More be done to detect and prevent these disorders by who work in the clinics for children aged 2 to 5 practical help and guidance should be given to parents, and doctors and health visitors should greater opportunities—if possible through case wor a psychiatrist—for learning something of the re and interpretation of emotional disturbances

Since respiratory disease has become the chief haz infancy after the neonatal period, its prevention sho a matter of great urgency The importance of fresh a good ventilation, the proper use of handkerchiefs, a avoidance of crowded cinemas, shops, and buses are principles which the centres should endeavour consta instil Similarly, they should be responsible for making p fully aware of the continued need for early prop against smallpox and diphtheria, as well as (in appr cases) of the value of tuberculin testing and who cough immunisation

As regards the prevention of accidents (now the g single cause of death in children aged 1 to 3) the memor s that every member of the child welfare team should e to bring home to parents the need to reduce risks onal instruction should be supplemented with group hing, and the fullest use made of cinema films, poster other visual aids. The aim should be to create a much ter awareness of the common causes of accidents and of without unduly restricting or frustrating the child may be prevented.

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[1] See *Publ Hlth Lond* 1955, 68, 51

ntil recently few children had regular medical super n between infancy and school age, and the frequency which unrecognised defects were found in school entrants cted unfavourably on the child welfare service. Thorough repeated examinations are particularly necessary (th p point out) for under-privileged children—th ature, the illegitimate, and those from problem lies. Mothers of such children must be given e uragement to attend the clinics, which should be the e for all the medicosocial work involved.

e first visit to the centre should be made when the child me 6 weeks old, and on this occasion he should have a ough medical examination. Thereafter he should be ined at the age of 6 months, 1 year, and 18 months, and equently at about the time of each birthday. Each ltation should allow ample time for discussion with the er of the manifold problems, large and small, of early hood.

o spread knowledge of child health the group would to see planning committees set up in health depart ts, including not only representatives from the centres but also the doctors responsible for the specialist services in the area, as well as general practitioners, nurses, and midwives. Indeed, in every aspect of child health there should be more coöperation between the people working in the centres and those with incidental experience of the problems of childhood. The health department needs the knowledge that the (family) doctor will have of the health of his group of children and he for his part will find increasing value in making use of a team of medico-social workers and in having behind him the resources of the health department.’

Reviewing the organisation of the centre, the memorandum points out that the task of distributing welfare foods should not take precedence over more important responsibilities nor absorb the time of trained personnel. If possible there should be enough ancillaries—clinic nurses, clerks, attendants, and voluntary workers—to undertake most of the less specialised duties. Finally, all clinic doctors should have special training in child health, in preventive medicine, and preferably in the methods of medicosocial research; and all nurses undertaking advisory work in the clinics should hold the health visitor's certificate. Such a staff, the group conclude, will enable the child welfare centre to continue as the principal focus of the preventive medical and educational work that is unremittingly needed to raise the standard of the health of young children.

# Parliament

## Horror Comics

the House of Commons on Feb. 22 Major GWILYM D GEORGE, the Home Secretary, moved the second ding of the Children and Young Persons (Harmful lications) Bill.[1] The publicity given to horror comics autumn had for the time being curtailed their lation, but it was difficult for parents and teachers e sure that children did not get hold of these comics out their knowledge, and the Government felt it ssary to ask the House to pass a Bill. It had been dered whether these publications could be pro- ted by proceedings under the law on obscene lications. But it appeared that as a result of judicial sions "obscene" had come to be regarded as being icted to matter relating to sex. It was unlikely publications which dealt with horror or violence d be the subject of successful prosecution under existing law.

urning to the new Bill he said that it defined the lications to which it applied in narrow terms. The lication must be a book or magazine which consisted lly or mainly of stories told in pictures. The stories t portray the commission of crimes or acts of violence ruelty, or incidents of a horrible or repulsive nature, lly, the stories must be so portrayed that the work whole would tend to corrupt a child or young person. e scope of the Bill was so limited that the Government ered that it carried no threat to the liberty of lishers, printers, librarians, or booksellers. It was, ny case, consistent with the long-established principle t it was the responsibility of Parliament, where ssary, to make special provision for the protection hildren and young people.

r FRANK SOSKICE said that the Opposition supported Government in this measure. We should lose a great l if we unduly lifted responsibility from the shoulders parents and teachers, but these publications would be d not in happy home surroundings but secretly ra by emotionally unhappy or mentally retarded dren. Sir HUGH LINSTEAD, on the other hand, ared that the House was being carried forward by rrent of public opinion to seek to do something by t of Parliament which an Act of Parliament could not ieve. As a result of publicity, except for a small p or two, it was now virtually impossible to buy ror comics. In a robust political community that s surely the way to deal with matters of this kind.

Mr RONALD BELL thought the Bill's main defect was that it applied only where the book, magazine, or other work consisted wholly or largely of pictures. Any publisher of horror comics who seriously wanted to get round that could do so. The intention to filter the mental experiences of children was dangerous. If children were to be protected in their youth from questionable influences, what kind of citizens would they be when they grew up without being taught to see things of which they disapproved? The only way in which a child could obtain strength and maturity of judgment was by being given an opportunity for judging between good and evil. Mr GEORGE THOMAS took the view that this Bill aimed at protecting not so much children as adolescents such as the young Serviceman who could hardly read. Sir DAVID ECCLES, Minister of Education, said that he had already asked school inspectors to see that there was an adequate supply of books not only in classrooms but also in libraries. He held that one of the best ways of killing the comics was to provide a decent alternative.

Mr SOMERVILLE HASTINGS, who for the past six years has been chairman of a large remand home for boys, said that as far as he could see all children, and particularly delinquent children, loved comics. Horror comics appealed to the primitive emotions of hate, revenge, and killing. One objection to these publications was that they tended to blunt the finer feelings. Another was that they were terribly frightening to children. There were terrible things in life which everyone had to face sooner or later, but he felt that children ought not to face them too soon.

Mr W. R. MILLIGAN, the Lord Advocate, agreed that the position had improved lately. But apart from the influence of parents and education authorities, the improvement was largely due to the public warnings given that legislation was to be introduced. If legislation were not proceeded with he was sure that there would be a resurgence of this literature. It was to be hoped that the mere existence of an Act of Parliament would serve as a warning and that there would not be many legal proceedings.

## QUESTION TIME

### Protection of Workers from Ionising Radiations

Replying to a question, Mr HAROLD WATKINSON said that the precautions taken at factories to protect workers from ionising radiations were carefully watched by H.M. Inspectorate of Factories, which was notified by the Atomic Energy Authority of all consignments of radioisotopes supplied by them to factories. The chief inspector had also issued an advisory booklet on precautions in the use of ionising radiations in industry. He was at present considering, in consultation with the chief inspector, whether in addition to the general requirements of the Factories Acts, more detailed special regulations would be desirable for factories using ionising radiations In all such matters he had the benefit of the expert advice of a radiological advisory panel, of the statutory advisory committee appointed under the Radioactive Substances Act, 1948, and of the Atomic Energy Authority itself As regards the projected atomic power stations, he was in consultation with the Minister of Fuel and Power regarding the measures that would be necessary for the protection of the health of the workers

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[1] See *Lancet*, Feb. 19, 1955, p. 412.

## Cadmium Poisoning

Mr **Harold Wilson** asked the Minister of Labour how many visits were made by H M inspectors of factories to copper refineries in Prescot Lancashire, to inspect the effects of cadmium fumes on the health of the workers, from 1946 to November, 1952, and since the latter date, respectively — Mr **Watkinson** replied Detailed records are not available before 1949 Between 1949 and 1952, seven visits were made by H M inspectors of factories to the copper refinery in Prescot Between 1953 and the present date, visits have numbered seventeen

Mr **Wilson** Is it not a fact that the Ministry did nothing to counter the effects of cadmium poisoning, which has killed quite a number of my constituents, until this matter was raised at the end of 1953 ?—Mr **Watkinson** No That is not so at all We have been watching this matter for a considerable time I do not accept the figures about the number of people who have been killed We have not had reported to us any deaths from cadmium poisoning Any such death occurring at premises under the Factories Acts would be notifiable as an accident in accordance with those Acts and satisfactory machinery exists for such notification The question of ill effects from long-continued exposure to small amounts of cadmium is being carefully studied in the light of the recent report prepared by a member of the staff of the Medical Research Council and other available evidence, both positive and negative Mr **Wilson** Is the Minister not aware that the reason for which some of these deaths was not reported to the Ministry was that this disease is not generally known about in this country ? I have obtained 6 death certificates from registrars showing cadmium poisoning to be the cause of death and these have not been notified to the Ministry Further, is the Minister aware that a post mortem done on the body of a constituent of mine showed that it was heavily filled with cadmium as a result of employment at this factory ?—Mr **Watkinson** If the right hon gentleman would let me have that evidence I will undertake that it will be considered when we look into Dr Bonnell's report We have only had it about a fortnight but it is being given urgent attention and I hope that we shall be able to make some progress

## Civilian Doctors in the R A F

Replying to questions Mr **G R Ward**, under secretary of State for Air, said that 114 civilian general medical practitioners were employed on part-time medical work by the Royal Air Force Remuneration varied according to the size of the station and the nature of the duties, which ranged from the medical care of a small station to the weekly inspection of canteens and workshops All rates were agreed with the British Medical Association 27 civilian doctors were employed on full time medical work by the R A F Their duties included routine medical examinations, diagnoses and treatment which did not necessitate admission to hospital, emergency attendance, and inoculations The salary was £1500, plus a Civil Service pay supplement of £35 It was reduced somewhat if a doctor was below the age of thirty five 34 part time civilian consultants and specialists were employed in the medical branch of the R A.F 6 received honoraria ranging from £360 to £750 a year Fees of the remainder were from 2–7 guineas for each consultation and $2^1/_1$–4 guineas for each session as member of a medical board

## Clinical Experiments

Mr **Peter Freeman** asked the Secretary of State for Scotland whether his attention had been called to experiments on 600 children, mostly orphans, conducted during the last three years at Bridge of Weir, near Glasgow, for testing a new vaccine against tuberculosis, and in how many cases permission was obtained from parents or guardians — Commander **J D Galbraith** Consent was given in every case either by the management of the homes acting *in loco parentis* for children in their care or by the parents where th [illegible] t members of the staff

## Dispensing Equivalents

Replying to a question, Miss **Patricia Hornsby-Sm** parliamentary secretary to the Ministry of Health, said that t Minister had noted that exactly similar preparations of so drugs, particularly penicillin, were manufactured by diffe chemical firms and stocked by dispensing chemists and th these preparations had different names He would not b justified, however, in authorising chemists to dispense prepa tions other than those prescribed The matter was prim one for the prescriber

Dr **Barnett Stross** Is the hon Lady aware that th are four or five oral and stable suspensions of peni which are exactly alike and certainly identical in their th peutic effects ? This may mean that a child with pneum cannot get anything to help it for a day or night wh similar preparation is available —Miss **Hornsby-Sm** Under the present code of the chemists it would be unet for a chemist to transpose one preparation for another t was ordered by the medical practitioner But there i reason why the chemist could not telephone the doctor a ask whether he would agree to change to the comp preparation Dr **Stross** Would the Minister make re sentations to the appropriate subcommittee of the Br Medical Association to give this matter full consideration Miss **Hornsby-Smith** The National Health Service do not authorise a chemist to substitute another prepar for one which is ordered and I do not think that gen the Minister could advise such a procedure

## Merit Awards

Mr **Beresford Craddock** asked the Minister of Health the identity of doctors granted merit awards from p funds was not published —Mr **Iain Macleod** replied In view publication of names would not be in the best inte of the National Health Service

Mr **Craddock** As the grants are paid from public fu what possible objection is there to publishing the name the recipients ?—Mr **Macleod** The objection surely that if it were known which consultants got class A, cla or class C awards, patients might think that, according which consultant was looking after them, they were different forms of treatment That would not be the because other factors than clinical ability are taken account That view, I think, has always been held by predecessors, and I believe it to be right

## Medical Man-power

Mr **James Johnson** asked the Minister whether, in v of the growing numbers of unemployed among British doct he would consult with the Secretary of State for the Col regarding their being engaged in the service of col governments —Mr **Macleod** replied The Secretary State for the Colonies and I already consult as necessar the needs of the colonial governments for medical staff, vacancies are, of course, publicly advertised in all approp cases Mr **Johnson** Is the Minister aware that there 200 applications for each vacant job today in the U Kingdom ? Further, there are some 61,000 people per do in Nigeria and things are worse in the Cameroons, where th is 1 doctor for every 71,000 of the population Would Minister ginger up matters and set up a working party investigate the question of seconding doctors to the Colo particularly to West Africa ?—Mr **Macleod** All posts advertised and any doctor can apply It is not within competence—and I hope that the hon Member does seek to imply it—to direct doctors to go to any partic area

## Salaries of Hospital Medical Staff

Mr **H W Bowden** asked the Minister what steps he ha taken to satisfy himself that the present salary scales wer sufficiently attractive to encourage young doctors to ent hospital service rather than general practice —Mr **Macleo** replied The salaries of hospital medical staff are a matt for the Medical Whitley Council in the first instance, b I know that the need to keep a proper balance in recruitme was an important factor in the agreement on increased salar reached by the council a year ago Mr **Bowden** Is t Minister aware of the difficulties experienced by many ho pitals in the provinces in obtaining and recruiting jun medical staff ?—Mr **Macleod** Indeed I am It would be mistake, however, to link those difficulties entirely wi problems of pay In many cases they arise because t spitals are remote or unattractive in themselves As far as y is concerned the agreement last year did a good deal to tore the balance which was upset by the Danckwerts award Mr J W Snow Is the Minister aware that it would be a at pity if the provision of practitioners for the countryside s in any way jeopardised? Is he aware that there are still ny rural areas under-doctored?—Mr Macleod Yes sir

### Identification of Babies

Replying to a question Mr Macleod said he was glad to e a chance to give the result of his inquiries into methods identifying babies in maternity hospitals The most mmon and satisfactory system seemed to be to attach a celet (or two bracelets) to the baby at birth (or to both ther and baby) with a corresponding label for the cot e sewing of a marked tape round the wrist seemed to be ple and effective Recent errors seemed to be due not defective arrangements, but to a failure to carry them out perly More elaborate arrangements would have no antages, and indeed might increase the possibilities of or The important point was that hospital staffs should be most careful in first making out the bracelet and label and bsequently checking them from time to time The bracelet thod was the general practice here and abroad but it had been laid down as absolutely standard The problem that d arisen so far had been because nobody looked at the celet and not because the bracelet was not there Clearly es could be festooned with bracelets but if nobody looked them the difficulty could still arise

### *Hospital Capital Development Schemes*

Replying to a question, Mr Macleod said that he knew no major hospital building scheme outside the existing 55-56 programme that was ready for immediate starting Any of those for which he had recently asked boards to ng plans to completion were ready to start before 1956-57 would consider whether it was possible to fit them into the 5-56 programme

### Nurses for Mental Hospitals

Replying to a question, Miss Hornsby-Smith said that number of *mental nurses* still showed a shortage of ut 10 000

## Medicine and the Law

### *Payment for Vaccinations*

During the smallpox epidemic at Halifax in 1953 e of the vaccinations were carried out by general ctitioners, to whom Halifax Corporation paid £443 fees based on the records of vaccinations Other cinations were carried out by doctors on the staff a local hospital under the National Health Service the corporation declined to pay these doctors A t case[1] was brought by one such doctor who sued the poration for £62 15s for compiling records of 251 cinations The Halifax county court found for this ctor and awarded costs against the corporation

Counsel for the plaintiff said that the Ministry's instructions vaccination had been given to the assistant medical er of health and were passed in turn to a doctor in the pital "It was in fact an invitation to the hospital doctors et on with the work. But they were in exactly the same ition as other G.P.s and no possible distinction could be wn between them" For the corporation it was contended at the vaccinations were administered within the plaintiff's ties at the hospital and by receiving salary for his job he d in fact been paid for the work Arrangements had been de between the assistant M.O.H. and a doctor at the hos tal, and when he passed the duties to the plaintiff the atter became the responsibility of the hospital manage- ent committee and not of the local authority Judge Myles rchibald in finding for the *plaintiff* said "I don't think hospital is the sort of place where you would expect this rk to be done."

The powers and duties of local health authorities with ard to vaccinations against smallpox diphtheria and her diseases are laid down in section 26 of the National ealth Service Act 1946

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1. *Yorkshire Observer* Feb 15 1955.

## In England Now

### *A Running Commentary by Peripatetic Correspondents*

The side-effects of national economy raise some pretty points of ethics.

The Vicar for instance takes a poor view of having to share his party line telephone with a secular subscriber Perhaps the ordering of a pair of kippers for Sunday morning's parsonage breakfast may be of doubtful spiritual significance to an eavesdropper, but Mavis Jones's frantic plea for an early wedding date is red hot stop-press news for the village Why, the girl left my *surgery only half an hour ago* But the disadvantages are not all one-sided The Devil shares the line as well whispering into the clerical ears the temptation of a dead cert for the 3.30 at Newmarket or eight draws that cannot fail for next week's treble chance Would the Vicar's soul be in less danger if he shared the line with the cloth of the other denominations in the district?

Then there is Mrs. Ugglethorpe who keeps the post-office and our general store It's the sort of place where a little bell jangles over the door as you enter The post office counter on the left stolidly proclaims the dignity *of Her Majesty's service, while the cards of aspirins,* liniment and backache pills flutter in the breeze by the window laughing scorn at the N H S Baby linen, groceries and paraffin jostle for pride of place, and if the customers shopping requirements are not sufficiently self revealing Mrs Ugglethorpe falls back on the switchboard in the kitchen The little levers stick a bit sometimes, and you can't help making two and two add up to four can you? Anyway our Bert runs the only taxi in the village and it is really rather public spirited to be getting it warmed up ready if Mrs. Hodges looks like coming off a week before her time

Every morning, of course the mailbag has to be sorted The Mudchester hospital management committee economise on envelopes and stamps, so the appointment postcards even tell you which doctor Mrs Clough is going to see, and when and where so it's up to you to guess the rest. That was how our village knew Mr Mason had T B It said CHEST CLINIC in big writing on the top The card for Doris Perkins to go to outpatients at 6.30 in the evening just shows that it does no good for young girls to be hanging round the harbour every night. Mrs. Ugglethorpe wagged her head knowingly

Ethics have to take second place to economy in these days.

* * *

The new social order is not so new The marauding Danes who built their squalid huts in the ruins of the great broch near Evie and the Arabs shivering among the fallen monuments of Baalbek knew our daily battle for warmth and shelter in the face of winter as we cower in part of a mid Victorian mansion This morning I looked from my window and saw that a thaw had come *Overnight the snow had slipped from the branches of the* cedar tree, and dark green patches showed on the lawn below I felt a sudden kinship with the age-old men who first lit ceremonial fires in earliest Spring hoping perhaps to coax an extra measure of sun to dry out their caves warm their shivering skin-covered shanks, and bring increase to their meagre crops. But one thing our ancestors were spared. They had no need every night to drain the radiator of a vintage car

* * *

The bus was listening attentively to the exemplary conversation of a mother with her daughter, aged about seven Every question was answered informatively reassuringly or amusingly as the occasion demanded and with completely unfrayed patience The mystery was resolved when it became clear that this was not a mother but an unmarried aunt bringing to the business a mind well furnished with modern views on child management and unfatigued by its daily practice Presently the conversation took an educational turn

I don't like French said the child

"Do you learn it at school?"

"No not yet but I don't like it"

But Jenny why not? You ought to be very good at French

Why?

“ Well, you hear Daddy and Mummy talking it And you often have a Swiss helper at home, don’t you ? And she talks French ”

“ All the same, I don’t like it ”

“ But darling, why not ? ”

The little girl was silent and went rather red At last she said in an undertone, looking out of the window, “ They have a very rude word for ‘ Yes ’ ”

* * *

A lecturer on the Third Programme lately suggested that some of the definitions in Johnson’s *Dictionary* are unconventional—e g , PATRON Commonly a wretch who supports with insolence, and is paid with flattery He set me thinking how the great lexicographer might have tackled a medical dictionary For instance, how about the following

PRACTITIONER, GENERAL An industrious fellow who treats patients who have been cured by the Specialists

BACTERIOLOGIST A fellow who is paid to report on colonial development

BANDAGE An appliance which the doctor hopes will stay in place until the patient gets outside

P U O Penicillin unleashed obliviously

SCALPEL. An instrument only slightly less sharp than the surgeon s tongue

COMMITTEE, HOSPITAL. An organisation wherein minutes are kept and hours are wasted

* * *

> “ The visitors were received by Mr Brown, the hall-porter, and conducted round the hospital by the deputy hall porter, Mr Smith , also included in the party were the chairman of the board, the matron, and the senior physician and senior surgeon ”

Although this version of the hospital hierarchy, offered in a report in our local newspaper, may shock Dr Ponderosum and Mr Fitzbrilliant, is it not correct ? First things first No-one from the most wretched casualty to the physicians and surgeons, not even the Queen herself, can enter the hospital without the concurrence, active or passive, of the hall-porter “ I want my mum, mister ” “ Where do I go for the fizzy-putic ? ” “ Good morning, sir ” to a passing member of the staff The spirit of the hospital, kind, fatherly, but firm, is embodied in his dignified person No hall-porter can be insignificant, and to a multitude the hospital is known by its porter

The night porter, though perhaps less impressive, is equally powerful—no reveller can stray in at 2 A M , no erring H P can slip past unobserved He reduces to abject docility a crowd of roughs escorting their friends who are bleeding from a rain of police truncheons, and the night casualty officer, alone and perhaps bewildered, may rely implicitly on his hoarse hints “ Dead, sir ” “ That one’s always coming up—a bit queer ” “ She’s bad at the other end ” “ I think it’s born ”

Let us face the salutary truth it is easier to replace a physician than a hall-porter

* * *

The following report from the minutes of an area council in this corner of the Dark Continent shows an engaging originality amongst councillors new to local government

“ , and finally resolved to urge the ******* local council to make bye laws to restrict women of this area from escaping from their husbands The question of establishing a market at Nkwanga was also discussed ”

* * *

From Magdalen bridge to Millbank
Routh’s dictum still holds good,
So may I softly chide you
In phil Adelphihood.
Your learned leader writer
Had not seen Collee[1] plain
Or sought to check his reference
Again and yet again
What better vesper versicle
To bless an author’s night—
“ My matter is impeccable
AND ALL MY REFS ARE RIGHT ! ’

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[1] In our issue of Feb 19, p 390, reference no 6 should be Collee J G *J R Army med Cps*, 1955, 101 (not 100), 46

# Letters to the Editor

## SANATORIA

SIR,—Thanks to modern antibacterial treatment, appear to be achieving a measure of control of pulmo tuberculosis which few of us expected to see in lifetime It is therefore important that we should re this new situation and mobilise our forces to their advantage Interest in this subject has shown it in recent articles and correspondence concerning relative merits of sanatoria, domiciliary care, ambulant chemotherapy

There seems to be general agreement that beds wil needed for the treatment of tuberculous patients some time to come The discussion appears to inv three main questions (1) Where should these beds situated ? (2) How ought the period of treatment be divided between institution and home ? (3) Who sh have clinical control of the beds ?

Advocates of domiciliary treatment, such as Dr Stra (Feb 19), hold that comparatively few beds are needed that they should be situated in a local hospital But difficult to see how this system can be justified as and fully equipped sanatorium beds become available length of general hospital waiting lists is causing hardship at one hospital, women with prolapse and incontinence have been told that they must wait two for admission because they require a “ luxury ” oper In such circumstances no one could advocate the treat of tuberculous patients in a general hospital if suitable torium beds were available for them in the same area. Stradling’s suggestion that tuberculosis sanatoria should “ diverted to other work ” invites a *reductio ad absur* because, if it were adopted now, the sanatoria would so dealing with general surgery and the general hospitals tre tuberculosis

Even with modern treatment it is doubtful whet drastic reduction of hospital care is in the best interes most patients In other progressive countries—for inst Canada, the U S A , and Scandinavia—it is a matter of to have sufficient sanatorium beds to ensure prompt adm of all newly diagnosed patients, as well as those with disease We in this country are now approaching su favourable situation , let us grasp its advantages and n satisfied with a make shift system of domiciliary treat Dr Stradling regrets “ the passing of the sanatorium ” says that we have an effective substitute in clinic manage But why must we be content with a substitute when we still have the genuine article ?

There is no doubt that the initial investigation, a ment, and initiation of treatment can be carried o more efficiently and expeditiously in a sanatorium in the patient’s home Early admission also en that the patient is not in contact with his family d the infectious period after diagnosis and before treat has got the disease under control Dr Stradling men the increasing importance of prevention, and, alth the dangers of infection are often exaggerated, it is difficult to justify the risk of treating an infec patient in his own home when a sanatorium b available Moreover patients learn more easily sanatoria to observe hygienic precautions, both specific instruction and from the daily routine

Rest is still essential, though antibacterial therapy is g reducing the length of the rest period Common sense d that it is far easier and better for most patients to rest recover in a well equipped institution devoted to that purp than in their own homes Progress is quicker under co trolled conditions, mobilisation can be carefully graded, the patient can be taught how to look after himself during still crucial two years after discharge The shortening of treatment period and the provisions of the Welfare S combine to make the acceptance of institutional treatm easier for the patient now than ever before Domici treatment, on the other hand, is much harder to control, success depends on the standard of the home, the coöpera of the patient, and many other variables not encount r hospital conditions. The advocates of domiciliary ment often work in areas where living standards are onably high, but social workers with experience of torium care are frequently dissatisfied with the conditions omiciliary treatment Too often they encounter house s on "bed rest" who get up and cook the meals or ules "up for 3 hours" who spend their evenings at the a.

ch has been made of the stigma attached to sanatorium ment In the U.S.A this has been largely overcome by ble propaganda, emphasising that patients who have treated in sanatoria can be regarded as having recovered can therefore be accepted into the community without rvations. There is, however, a simpler solution just as berculosis officers have become "chest physicians" so "sanatoria" become "chest hospitals"—a term devoid y stigma

ther alleged disadvantages of sanatorium treatment include ing difficulties due to distance and the adverse psycho al effects of isolation association with other tuberculous ents, and the restrictions of a regular routine There is truth in all these things but until recently they were rded as a small price to pay for the benefits of sanatorium . Much can be done to overcome them, and the tion which many ex patients continue to feel for their toria is good evidence that these objections are not perable

robably the most important obstacle to the proper of sanatorium beds is the reluctance of the chest ician to lose clinical control of his patients while are in sanatoria Dr Stradling hits the nail on the d when he says that continuity of management is factor of vital importance in a long term illness olving many social and psychological factors not to tion differences in clinical opinion There is no bt that the physician who has to undertake the long care of the patient ought to have the major say in ning that patient's management and should ideally in close touch with him during his stay in the sana ium Unfortunately this principle has often been lected and an independence almost amounting to lry, has sometimes grown up between clinic and torium

ut this is a problem which can be overcome given d will on both sides. Many sanatoria are within reach the centres of population which they serve and it is n possible for the clinic physician to retain control his patients and to take part in clinical conferences h the sanatorium physician and the surgeon at which or questions of policy are decided The sanatorium sician has certain advantages over the busy clinic sician he is better able to observe and study his ents and has more time to get to know them and problems but together they are in a stronger tion to treat the whole man than either can attain e. Such team work is understood and appreciated the patient, it increases his confidence and it does h to persuade him to accept and follow advice enever possible the sanatorium physician should also p in the work of the chest clinic thereby acquiring ler outlook and an added interest This system is, course in operation in many areas and has proved its th. Its universal adoption would undoubtedly hasten day when both sanatoria and chest clinics become ndant

A F FOSTER CARTER.

mpton Hospital Sanatorium
Frimley Hant

SIR,—It is impossible to give an adequate answer to Stradling in a short letter but I would like to some points in support of Mr Temple's excellent ter of Jan 8

(1) The closing of the Trudeau Sanatorium must be regarded th sentimental regret) as a result of the enormous provision free sanatorium treatment in the U.S.A which was almost chievable twenty years ago. Consider the plight of the ivate sanatoria in this country

(2) The countries States and provinces which have made real progress in a campaign of tuberculosis eradication are those with adequate hospitals and sanatoria They did not believe in waiting lists but had waiting beds and used them. Ontario with the tuberculosis death rate down to 6 4 per 100 000 is still adding beds

(3) Tuberculosis is still an infectious disease Good training of the patient anywhere will reduce the risk of spread of infection but in my experience this training takes time and it can be carried out most safely and economically on a group basis in a sanatorium

(4) In a sanatorium which has not discarded the old basic sanatorium principles to which modern treatment is a supplement, not an alternative there is no difficulty about psychological readjustment to return to employment. The sanatorium patient has the advantage of physical readjustment also His rehabilitation should begin on the day of admission

Dr Stradling's five year results for 64 domiciliary treated patients are very good (though one must quibble at the survivals in groups of 11 or 12 being expressed as percentages) It must have required a considerable amount of consultant specialist and nursing time to achieve these results This time could surely have been more economically employed with the patients congregated in the sanatorium

The population of a well run sanatorium is not a collection of miserable creatures crawling about in uncongenial surroundings. It is a community of high morale where adaptation to the limitations imposed by pulmonary tuberculosis is rapidly acquired Apart from a few misfits the reaction to corporate life is good and many patients leave the sanatorium better citizens

Domiciliary treatment of tuberculosis was introduced as a matter of expediency when waiting lists were long but to adopt this expedient as a reason for abolishing sanatoria when such a policy would mean in industrial areas the treatment of the case in overcrowded and relatively insanitary conditions would seem to me the height of folly

Many of the views I have expressed are the result of personal experience of both domiciliary and sanatorium treatment from the patient's point of view

Cheshire Joint Sanatorium
Market Drayton
Salop

A CLARK PENMAN

SIR,—I agree with Dr Stradling that the time is ripe for an all-out drive against tuberculosis now that eradication is practicable The remarkable decrease in deaths from tuberculosis and the recent occurrence of empty (female) beds in some sanatoria are both indications that tuberculosis is at last on the way out (We need not be alarmed at the maintenance of notification rates which are related to better case-finding—mainly by mass radiography ) The factors concerned in this achievement are :

(1) Epidemiological—i.e those conjectural causes which normally bring epidemics of infectious disease to a close and which are related to their duration number of susceptibles at risk &c

(2) Environmental—i.e housing nutrition health education &c

(3) Active preventive activities including case-finding contact examination and B C G inoculation

(4) Treatment including the sanatorium regime chemotherapy minor collapse measures and major surgery

Of these we exercise no precise control over (1) and we must admit that the steady fall in death rates in the past fifty years or more has (except very recently) been associated almost entirely with (2)— the amelioration of social conditions Of late no doubt this fall has been increasingly influenced by (3) and (4) and the accelerated decline since 1948 must it seems be due to streptomycin, P.A.S., and isoniazid

The main function of tuberculosis dispensaries, as envisaged by the 1912 Astor Committee, was prevention, and prevention should still be the first concern of chest clinics

There is ample scope for them in tracing contacts of notified cases, in examining contacts of Mantoux positive children and adolescents, in the wide scale use of B C G , and in similar activities Our long term plan must be to banish not only tuberculous disease but tuberculous infection from the community, and this will ultimately involve large scale repeated Mantoux testing of the whole population (when, incidentally, B C G will become an anachronism), and these activities will obviously have to be centred at the chest clinics

Owing to pressure on sanatorium beds after the war, tuberculosis beds were opened in general hospitals and most chest clinic physicians organised domiciliary treatment The fact that there is a diminishing call on these beds is posing a new problem to those engaged in this work, and the lurking fear that they may be underemployed may explain this correspondence It has to be faced that, with diminishing material, the tuberculosis services must sooner or later undergo some reorganisation and reintegration, but this will not be made easier by factional squabbles, or by the denigration of one part of the service by the other

With regard to general hospital beds, no-one can deny that they have been of value , but they were diverted from other uses, and I believe that the physicians formerly in charge would welcome their return to their original use, particularly since everywhere there is a shortage of geriatric beds

Some of us still believe in the sanatorium régime as a basis for the cure of pulmonary tuberculosis

Fresh air, graduated rest, and graduated exercise are not always easily provided by a general hospital Moreover, organised leisure activities—occupational therapy, inter-ward games, ward entertainments, whist-drives, &c —all tend to make the patient resigned to his long stay, and in a well run sanatorium contribute to the high morale not easily attainable elsewhere Some 30–40% of sanatorium patients undergo major surgery, for which these institutions are equipped and in which their staffs have had long experience There is every argument for integrating surgery and chemo therapy with the sanatorium régime, and, in particular, for insisting on a long period of convalescence in order to avoid relapse—still a feature of pulmonary tuberculosis despite modern therapy As the pressure on beds becomes less, sanatoria might well carry this process, as in the past, to the stage of rehabilitation by graded work, so that patients leave (except for a short period of psychological readjustment) fit to return to their jobs Another feature of the specialised work of sanatoria is the large volume of laboratory work undertaken by them, mainly in relation to culture investigations and resistance tests—specialised work which would over tax a general hospital laboratory Many sanatoria have also recently set up a respiratory-function department, again a highly specialised study By all means let chest physicians retain a certain number of beds for urgent admissions for diagnostic and similar purposes, but let sanatoria continue to carry out the work in which they have specialised for so many years

I agree with Dr Stradling that sanatoria need not be buried in the country—although I think many patients appreciate such surroundings when they get there I do not consider daily visiting necessary or even wise—a point of view which we in sanatoria teach our patients to share

I admit again that domiciliary treatment, if it includes chemotherapy and pneumoperitoneum, may achieve a useful purpose , but having seen some of its distressing results I cannot agree that domiciliary artificial pneumothorax is wise treatment Long-term chemotherapy of the chronic case can well be carried out in the home—but preferably after the sanatorium has achieved maximum improvement The value of ambulant chemotherapy of the recent case, as suggested by Pritchard, can only be de[illegible] by long-term controlled trial

Possibly some chest clinic physicians over emph the clinical aspects of their work—reflecting, I th the exaltation of clinical over preventive med imposed on us by the architects of the National H Service Advances in the fight against tubercul have in the past been due to prevention, and with t present full exploitation of existing drugs and surg further progress must, it seems, come from prevent rather than from the clinical field Would not c clinics be wiser to concentrate on this aspect of th work ?

Collindale Hospital,
London, N W 9

W E SNEL

SIR,—Your correspondents have been chiefly cerned with the treatment of pulmonary tubercul I should be grateful if I might comment on future of sanatoria for patients suffering from o diseases

Most sanatoria have progressed a long way from th prototypes, because the requirements for the treatme tuberculosis, particularly if the whole range of the dis is included, have increased so much They have become well staffed and well equipped hospitals w special function is to meet the needs of patients who require treatment over a period of months Ev beds were available in general hospitals for many of th patients, the atmosphere and surroundings of a ge ward and the continuous pressure to accelerate the t over are unsuitable for them The advantages of a w in an open air country hospital are that the temp slower, and more conducive to the patient's peace mind The change to rest under better hygienic condit improves their physique, often remarkably Ther no lack of visitors if suitable hours and trans are arranged by the hospital authorities, and slower turnover enables personal relations bet patient and patient and staff and patient to count more

Though the ward routine is primarily organised for t ment, rehabilitation and recreation also play their part patient is not in his ward all day These conditions do reduce efficiency of treatment and even offer advant There should be no sepsis because the wards can be open light and air Patients tolerate major surgery better bec they have preliminary constitutional treatment

The use of such long stay hospitals has up to the p been almost confined to orthopædics and tuberculosis. doubtful if the number of adult long term beds for pædics in the country is sufficient Other well known c for long-term treatment are the plastic surgery unit at Victoria Hospital, East Grinstead, and the paraplegic at Stoke Mandeville Some sanatoria are already t patients with non-tuberculous lung conditions.

Tuberculosis hospitals have been staffed on a very cath basis, drawing their consultants from teaching and univer centres and from neighbouring towns, in addition to sultants working full time at the hospital Thus dep mentalism has been avoided and it has been possible draw patients from a wide area Though there are advant in having some general medical and surgical beds in th hospitals to meet local needs, their chief work should cont to be for patients who can be cured or improved by long t treatment and who will not be cured unless they get treatment For these there should be a wide catchment and the chief work of the hospital should be to serve region

For this reason the regional boards should be prepar to provide the same administrative arrangements f the special units of these hospitals as they ha in the past for tuberculosis If these conditions were be fulfilled, the sanatoria of the future, as the needs tuberculous patients decrease, would still function open air hospitals, with a wider scope, and no le useful work

Black Notley Hospital,
Braintree Essex

M C WILKINSO

## TREATMENT OF ENURESIS

SIR,—Dr Symonds draws attention (Feb 26) to th acing of children as a cause of neurotic illness It this reason that I advise my patients to wait fo 3 years before considering a second baby It is at age of 3 that the child begins to demand a broth ister, and, though at first he notices the change nposition of the family picture where all viewing directed to a new centre he soon takes on the little father The younger child, bound up in ther alone cannot comprehend the reduced intere t subordinate figure

A greater factor, however, in emotional illness is the ient's position at the top of the family tree Every eral practitioner knows how often the mother and first infant are on his doorstep About her eagerly uted firstborn she is unduly anxious and ov fective and she lacks experience. The first child refore receives a welter of care, and is the only one o will receive 100% of his mother s affection and s ch anxiety He it is who suffers from a situation less gnant for any aftercomer, and in nine cases out of it is possible for the doctor to diagnose the prim ture of his patient from a consideration of his nptoms alone

ford. R N C SMITH

## B C G VACCINATION

SIR,—Professor Heaf (Feb 12) says that there is ng evidence that B C G increases resistance against rculous infection although statistical proof is difficult obtain" He admits our ignorance of allergy and munity in tuberculosis, but he *also* says " these nowledged advantages of the vaccine are sufficient justify its use" Are these advantages so generally nowledged? The fact that the vaccine is readily ministered and cheap is not so very important the damental question to which we do not know the wer is whether a positive skin reaction is really very portant in immunity to tuberculosis After all we have r diseases in which positive skin reactions occur but o not know that it has been suggested that they mean munity For example does a positive Frei test indicate immunity to lymphogranuloma inguinale, and does ou s reaction indicate any immunity? Are we really tified in asking parents to submit their children to ctions which may in a significant proportion of cases duce unpleasant local reactions and have a risk, ever slight of causing general disease, when we have lly no sound knowledge of its good effects.

ome of us in the older group are perhaps overanxious remember previous campaigns for the use of B C G remember also the movement for immunisation inst scarlet fever some 20 years ago now I think mpletely discarded and we remember earlier attempts ith much enthusiasm) to use vaccines against whooping gh whose value is now known to have been nil

I write because I want to be convinced If B C G is a d thing then by all means let us use it but I would e to know more about the 'acknowledged advantages the vaccine We do know of the solid advantages of unisation against diphtheria and therefore some s are extremely hesitant about any procedure which ht prejudice that immunisation It is admitted that ny authorities of high standing are sceptical about C G and that indeed in recent years the sceptics have ome more vocal Is there an answer to this? It has n pointed out by Dr McIntosh senior chest physician Dundee that in that city there was a very considerable line in tuberculosis mortality in 1947–51 and he points t that if B.C.G had been used on a wide scale in 1947 re would have been a strong temptation to credit it h the good result Can Professor Heaf convince those f us who hesitate on the brink?

I am, of course expressing a purely personal doubt and not that of my employing authority

*rington.* R C WEBSTER.

## BEHÇET S SYNDROME

SIR—When one has collected a series of cases of a rare disease it is a pardonable error to suppose that the condition must be commoner than is supposed and that others are missing the diagnosis We are impelled to defend our dermatological colleagues from the charge of failing to diagnose Behçet's syndrome

In their interesting paper (Feb 19) Dr Phillips and Dr Scott give a useful account of aphthosis of the mouth and vulva with its other possible complications The dermatologist however is only too familiar with the incomplete picture of aphthous stomatitis the common occurrence of which should be emphasised as opposed to the extreme rarity of involvement of the vulva or the eyes

The association of lesions of the mucosa and skin with various inflammatory reactions of the eyes has long puzzled dermatologists Juvenile cataract with atopic eczema (Werner s syndrome and Rothmund s syndrome) is due to a combination of genetic defects,[1] but the eye lesions of sarcoidosis and Reiter s syndrome have no obvious explanation. The pemphigus and erythema multiforme groups, on the other hand attack the mucosa and skin with equal severity; and in these the graver the illness the more probable is involvement of the conjunctivæ mouth and genitalia But in bringing the erythema multiforme group—which includes the Stevens-Johnson syndrome—into the differential diagnosis of Behçet s syndrome, Phillips and Scott have made matters unduly difficult Erythema multiforme when it affects the mucous membranes, produces superficial sloughing of the whole mucosa, and true painful aphthous ulceration is never *found in this condition. They are incorrect in stating that the* Stevens-Johnson syndrome occurs as a single attack recurrent though admittedly not cyclical attacks are not uncommon.

One disease which they do not mention, that could be confused with Behçet s syndrome is benign mucous membrane pemphigus We have tried to clarify the diagnostic criteria of this condition[2] which must sometimes be missed through the patients receiving only a specialised examination by the gynæcologist Ocular pemphigus, as it is also called, produces chronic recurrent ulceration and scarring of the conjunctivæ mouth, and vulva; and though there is no doubt in our minds that it is a distinct entity affecting the elderly it resembles Behçet s syndrome closely enough to be important in differential diagnosis.

Finally we are a little mystified by the statement that Behçet s syndrome may eventually be placed among the collagen diseases The ætiology of Behçet s syndrome may be obscure but one would require evidence of involvement of collagen in the disease process before throwing it into this modish ragbag

Rupert Hallam Department of
Dermatology, Royal Infirmary
Sheffield

R E CHURCH
I B SNEDDON

SIR—The extremely interesting article by Dr Phillips and Dr Scott prompts me to record the following case of Behçet s syndrome

A married man, aged 33 had an inflammation of his left eye in August 1952 which cleared up with penicillin eye-drops The following month the inflammation recurred and later spread to the other eye He was then found to have a bilateral iritis

In October 1952, he received a 10-day course of oral cortisone and his vision which had previously been blurred became normal The iritis relapsed soon after treatment was stopped and was not improved by a course of local cortisone therapy After that the condition of his eyes deteriorated until he became completely blind owing to a bilateral iridocyclitis.

In November 1952 he first had very painful ulcers on the inner aspects of his lips buccal mucosa tongue and palate and he brought these to the notice of the ophthalmologist, but they were not considered to be related to the eye condition Since 1952 these oral ulcers have recurred at frequent intervals and resolved spontaneously

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[1] Carleton, A *Brit J Derm* 1943 55 83

[2] Church R E Sneddon I B *Ibid* 1953 65 735

Since December, 1952 he has had frequent episodes of painful pink raised round lesions in the skin overlying both tibiæ, which *from the wife's description appear to be almost* certainly erythema nodosum

At no time has he had an attack of monarticular arthritis, but during the period of his illness he suffered from recurrent pains in both shoulders, elbows, and wrist joints, and also in his back I first saw the patient in general practice in May, 1954, when he consulted me because of a painful ulcer of the scrotum He told me that he had his first scrotal ulcer one month previously which cleared with local treatment

In September, 1954 he had a further episode of scrotal ulceration and at this time there was one ulcer about $^1/_2$ in in diameter and extremely painful

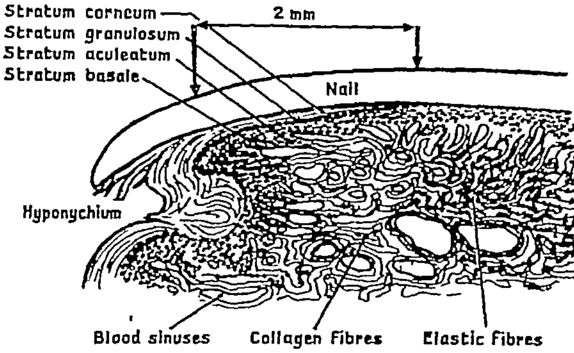
In view of the association of iritis, oral and scrotal ulcers, and erythema nodosum I considered him to be a case of Behçet's syndrome This diagnosis was not made at the eye hospital he attended, as the patient had not told them of the erythema nodosum or scrotal ulcers

Regarding ætiology, this patient had never been in the Middle East, nor, to his knowledge, suffered from bacillary dysentery I mention these two facts because most cases have been reported from the Eastern Mediterranean region, and Karani[1] described the case of a soldier with Behçet's disease, the onset of which followed an attack of bacillary dysentery in Egypt

Broughton, Manchester S SHUBERT

## ONYCHODERMAL BAND

SIR,—Last year, following an article on white nails by Dr Terry,[2] you were kind enough to publish a letter from me about a man with white nail-beds Soon after that, my patient died, and, through the interest of Dr D S Wilkinson, of St Thomas's Hospital, Dr I W Whimster sent me a most detailed account of the histology of the nail bed, together with the sections from which I have drawn the accompanying diagram I thought this might be of interest in view of Dr Terry's latest paper on the "onychodermal band," in your issue of Jan 22 As can be seen, the band is clearly demarcated histologically by the absence proximally and presence distally of the stratum granulosum with its cornified layer. There is also very little elastic tissue beneath the terminal part of the nail, as well as under the lunula, whereas, beneath what Dr Terry describes as the "main pink zone," it is abundant, though this is not clearly shown in the diagram It is interesting to speculate on the reason for this, as one would casually be inclined to deny the necessity for it under the firm support of the nail it may be simply due to what Dr Whimster tells me is the embryological difference in origin of the two parts



Kingston-on Thames
Surrey CHARLES STEER

## RELIEF OF PAIN IN INCURABLE CANCER

SIR,—With reference to my article (Jan 1), it has b pointed out to me that doubt might arise concerning preparation of the phenol solution

This solution is prepared freshly each week by dissolv 1 g of phenol crystals in 20 ml of glycerin or propylene glyc The solution is kept in rubber capped bottles Before injecti 0 1 ml of sterile water is added per 1 ml of the solution, the two are well mixed

Recent observations have shown that where the pa has had pain for less than six months the addition of st water is apparently unnecessary Furthermore, lower d of the phenol glycerin mixture itself are required, and 1 ml of 1 part of phenol to 20 of glycerin suffices After months of pain, resistance rises and the dosage needs t correspondingly increased above 1 ml of solution.

Rochdale, Lancashire R M MAHE

## CHLORPROMAZINE AND GASTROSCOPY

SIR,—In his letter of Feb 5 Dr Morton Gill rec that nausea and retching were common after gastrosc and were sometimes so severe that the patients had be confined to bed By the use of chlorpromazine endoscopy, these symptoms were largely preven I do not know what preliminary anæsthetic Dr uses, but I have found that with the administratio 'Pantopon' (papaveretum) and atropine I have had very rare cases of nausea and retching, and these certainly never been so severe as to keep the pa in bed

My reason for writing, however, is not this comp tively trivial point, but rather the timing of the inject of chlorpromazine I also give it in 25 mg intramusc doses, but *before* the gastroscopy and in conjunction pantopon This method avoids the pharyngeal refle nausea and the vomiting on the introduction and drawal of the gastroscope, which is the most trouble part for the patient The subsequent discomfort, w in my experience is not very common, is also minimi

Madrid L GANDARA MAZPUL

## ELECTROCARDIOGRAPHIC CHANGES AFTER GASTRECTOMY

SIR,—In his article last December[1] Dr Brotma dealt with postprandial electrocardiographic (E.C changes following gastrectomy Earlier, Dr Pulvert had attempted to relate these changes to auton effects which, presumably, were exaggerated in persons following gastrectomy Since I showed in 19 that such electrocardiographic changes occurred in normal person without being associated with sympto it seems to me that the employment of the E C G chan as an indicator of any sort of occurrence related symptoms is illogical[4] Furthermore, the assumpt that the E C G changes are related to autonomic chan —though it may be quite correct—is unsupported evidence

The E C G changes which follow meals are complex 1938 *I concluded that there was a postprandial* T wave chan which was *not* related to change in cardiac rate or positi and I tentatively suggested that such changes might be importance in the clinical interpretation of E C G.s It equally clear that some T wave changes which occur po prandially *do* result from changes in cardiac position and rat The former type can usually be distinguished by the corre ponding change in the QRS axis which, despite Brotmacher statement to the contrary, does appear in his figures (mo distinctly in fig 3)

In the investigation of changes in the E C G after the ingestio of food it is impossible to be certain that the patient's body in precisely the same position for any two observations Th

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Karani S B *Proc R Soc Med* 1953 46 45
*ancet*, 1954 1 757

1 Brotmacher, L *Lancet* 1954, ii, 1307
2 Pulvertaft C N *Ibid*, 1954 i, 325
3 *Amer Heart J* 1939, 17 725
4 See Gardberg, M *Lancet* 1954, i, 1080

ree of error can be minimised but not eliminated A slight nge in position of the body coupled with filling of the mach or even without this, or a different respiratory tion of the chest can cause an important change in the T e Again QRS changes give a clue to the existence of this or A slight change in the QRS from whatever cause s rise to an important secondary change in the T wave

nvestigation of the effects on the E.C.G of the intro tion of water air, and food into the stomach in those o have and in those who have not undergone gastrec y requires much more critical attention to all the ors involved Such an investigation is under way here Brotmacher s conclusion regarding the role of hanical distension is probably correct but not new postprandial E.C.G changes distension of the gastro stinal tract cooling, and biochemical or autonomic ors may all play a part

ew Orleans,
uisiana, U.S.A. MANUEL CARDBERG

## NCTIONAL SYMPTOMS OF ORGANIC DISEASE OF THE BRAIN

IR,—I was most interested in Dr Blake Pritchard s le (Feb 10) I fully agree with him that organic es must be carefully investigated and excluded before ng the diagnosis of hysteria The following case trates this well

woman, aged 32 was referred by her general practitioner a five-year history of tiredness, headaches, muzziness fear of falling There had been a few black outs. Sh been seen at a neurological hospital and referred for hotherapy She was discharged as uncoöperative and admitted as an inpatient at a neurosis hospital She was n discharged as a chronic hysteric and was admitted to her neurosis hospital, where she stayed for six months here was a full physical examination attempted. When ame to my outpatient clinic she had been unable to work ghteen months What struck me was her quiet behaviour ncerity of her wish to get back to work her excellent ng record and the fact that her mother reported a ite change of personality at the time her symptoms first n. She had held one job for about sixteen years and her loyers had been keeping her place open for her Electro phalography suggested temporal lobe epilepsy and her investigation was advised

ould it not have saved trouble for the employers and general practitioner and much anxiety and self ching for a patient stamped as an uncoöperative unintelligent hysteric if such investigation had been ed out to begin with ?

ritish Hospital for Functional
rvous Disorders London, N W 1 HILDA C ABRAHAM

## STERILISATION OF SYRINGES

IR,—It is important that Dr Rollason's letter of 19 should be answered since the inference is made assembled syringes can be successfully sterilised in autoclave The principle behind the use of autoclaves sterilising depends upon the penetration of saturated am to all surfaces In an assembled syringe the tration of steam to the inner surface of the barrel or er surface of the plunger is clearly difficult and is ther complicated if (1) the needle is mounted and the assembled syringe and needle are placed in ss or metal container Dr Rollason is therefore ending upon dry heat alone which under the con tions stated would not be sufficient to sterilise many res. If Dr Rollason likes to carry out the simple eriment of placing dried spores in the bottom of the rel with the plunger in position he will soon be con ced that autoclaving under these conditions is not ptable as a method The problem is admirably dealt h in Walter s book on the Aseptic Treatment of unds[1]

In a busy syringe service it is necessary that labour and cleansing processes should be simplified Excellent as the Vim syringe is, it suffers from the serious disadvantage that the barrels are not interchangeable and this means that plungers and barrels must be kept together This is *too large a feat to be practicable* when 000 syringes are being sterilised daily A further disadvantage in common with all metal and glass syringes is that repeated heat causes the solder, used to cement the parts together to disintegrate, and eventually leakage occurs.

Central Laboratory
Portsmouth

E M DARMADY
K E HUGHES

## MELANOPHORE-EXPANDING ACTIVITY OF HUMAN PITUITARY GLAND

SIR —Dr Hudson and Dr Bentley (Feb 10) have shown that a melanophore-expanding hormone has been prepared from human pituitary Their laboratory animal was *Xenopus lævis* which is the one amphibian known[1] to respond to adrenaline by expansion of the melanophores Their technique for extraction would not have destroyed any adrenaline present and control assays were not mentioned. It seems possible that the result obtained may have been due to adrenaline

For the estimation of melanotrophic activity the species of choice is the tree frog (*Hyla arborea*) which will give a response to 0 25 ml of normal human blood diluted 40 000 times. This corresponds roughly to $10^{-4}$ µg of a commercial preparation of corticotrophin (Frazer unpublished)

Charing Cross Hospital
Medical School,
London, W C.2

J F D FRAZER.

## POST-PREGNANCY OSTEOPOROSIS

SIR —Dr Nordin and Mr Roper whose article under this heading appeared last week were wise in adding A Syndrome ? for I think it falls into the syndrome to which I have given the name Shaw Reade '[2]

The authors write: As our patients have been observed for only a short time and the period since delivery differed in each case our data provide little information on the course of the condition We cannot be sure what effect if any hormone therapy has had on the patients' Earlier they say that the purpose of this report is to suggest that the association between the osteoporosis and the pregnancy may not be fortuitous ' I note that the patients were admitted for investigation and the symptoms improved spontaneously but their conclusion that these findings are all compatible with a diagnosis of osteoporosis and strongly against one of osteomalacia ' is in my opinion based on very incomplete knowledge

Why were three of the four patients submitted to biopsy ? They ought to have known what they proved—that this procedure was fraught with danger (I have known of two patients who died under anaesthesia during exploration of a benign and quiescent lesion) that it could yield little valuable evidence and like radiography does not permit of accuracy in diagnosis Are they to be commended for stating Since all four patients developed the condition in close association with childbirth and have been improving steadily ever since we suspect that there may be some connection between the condition and childbearing ?

The authors show by the use of the term codfish vertebræ that they have failed to note that the essential feature in their cases is probably the expansion of the discs which have compressed the vertebræ—these having reacted to the pathological changes in the discs I have clearly indicated in many of my publications that bones

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[1] Walter C. W Aseptic Treatment of Wounds New York, 1948

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[1] Burgers, A C J Boschman Th A C van de Kamer J C *Acta Endocr., Copenhagen* 1953 14 2

[2] *Medicine Ill* 1951 8 395

have a way of reflecting the pathological changes of adjacent structures, therefore I am not prepared to accept that "the absence of decalcification and pseudo fractures in the limb bones, despite the codfish vertebræ [and the crush fractures], pointed to a diagnosis of osteoporosis rather than osteomalacia"

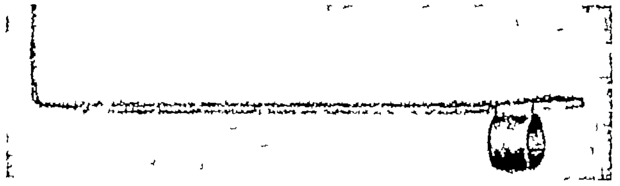
Birmingham JAMES BRAILSFORD

## VALVOTOMY KNIFE

SIR,—I was very interested to read the description of the new valvotomy knife devised by Mr Lentin (Jan 15)

At the beginning of last year my registrar, Mr N A Shah, and I devised a rotating valvotomy knife which was made for us by Messrs W R Swann, of Sheffield This, I think, has certain advantages over the knife described by Mr Lentin

The ring attachment is placed around the terminal phalanx of the index finger, thereby allowing flexion of the finger during the manœuvre of splitting the valve, and ensuring apposition of the knife blade to the finger The blade (on a rotating flexible shaft) is attached to the ring in such a way that it can be inserted into the appendage with the cutting edge sideways, it is then rotated 90°, and locked in that position to enable the anterior commissure to be cut with the finger flexed and the hand supinated The posterior commissure can be cut with the hand pronated The knife blade is against the finger tip during the whole manœuvre, and is easily controlled On withdrawal, the knife is rotated through 90° to its original position, and locked



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Leicester BETTY V SLESSER

## THROMBOPHLEBITIS FOLLOWING INTRAVENOUS INFUSIONS

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Thrombophlebitis after saline infusions is very often met with in cases of cholera, and I have been unable to prevent its occurrence by repeatedly autoclaving and cleansing the apparatus, and by taking full aseptic and antiseptic precautions My experience is rather different from Mr Jones's

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To ensure greater asepsis I stopped cutting down and used instead a Rogers needle, but the incidence of thrombophlebitis remained unaltered I found that the condition was almost certain to develop if the transfusion had to be continued for a long time Many of the severe, suppurating responded well to oxytetracycline, but most of tho grossly swollen hard brawny legs (without supporat showed practically no response to that drug

Of more than 3000 patients whom I have treated w intravenous infusions, scarcely 30% escaped this exce ingly troublesome complication Clearly there is a gre need for further research into the ætiology, meanwh the use of Baxter latex tubing appears to offer the practical solution to the problem

Civil Hospital, Putao,
Kachin State, Burma. RANENDRA BANER

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[1] Jones P F *Lancet* 1954 ii, 970

## CHEMOTHERAPY OF LEPROSY

SIR,—As one who for the last seven years has wo in Eastern Nigeria and applied the results of Dr Lo researches to several thousands of cases of leprosy, I I must join issue with Dr Jopling in his conten (Jan 8) that Dr Lowe's "results apply to Africans particularly well-favoured part of Africa and exceptional"

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We had plenty of active lepromatous cases, some advanced, and the vast majority were rendered clinically bacteriologically negative by carefully applied courses oral dapsone Dr Jopling is perhaps unfortunate in tha may have among his patients many in whom the d has begun to regress either spontaneously or after irregular treatment, leaving secondary neural and changes These are always the most difficult and un factory to treat, and we had our share of them in Ni They do suffer badly from reactions, but then the maj of sulphone treated lepromatous cases do It is a certainly a part of their cure, and usually the earlier t ment is initiated the less severe the reactions I have impression that the normal course for an untreated leprom case to follow is frequent reactions with steadily incre skin and nerve damage and gradual dying out of the b spread over variable periods of perhaps ten, twenty, or th years A case treated in the early stages by dapsone se to have a somewhat similar course compressed into ab five years, but with moderate and decreasing reactions sometimes (but not always) much nerve pain steadily decre ing and leaving little or no nerve damage, according to h long the disease has been present before treatment was beg

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on W1

B WHITCHURCH HOWELL.

## IMPOTENCE

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SIR,—Arising out of your annotation of Feb 19 it may be of interest to record that in a recent discussion with the medical staff of the hospital in Sulaimaniya, which is the principal centre for an urban population of 60 000 and the province of 250 000 the doctors mentioned that they saw very little cancer of any kind, except rodent ulcer which is common This statement was confirmed by a German woman gynæcologist of long experience, who has been working in the area for the past two years, and who said that cancer of the cervix and body of the uterus is rare In their view the explanation was to be found in the diet of the Kurds The surgeons, who were men of great clinical experience could recall only one case of cancer of the lung, and they did not think that they were likely to miss this condition for, although post mortem examinations are relatively rare, they are well equipped for diagnosis and are on the look-out for it If it is true that there is practically no cancer of the lung then I think that some other explanation than cigarette-smoking must be found for nearly everyone I saw, both men and women smoked cigarettes heavily

Department of Human Ecology
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## CIRCULATION OF THE UTERINE WALL IN PREGNANCY

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To the pure clinician, laboratory observations are of value inasmuch as the bedside application of procedures formulated from new concepts aid in the perfection of physiological function or relief from pathological states

Whether toxæmia is due to one or more of the host of its theoretical causes I am unable to say but certain simple observations relating to both myometrial circulation and the incidence and control of toxæmia may be of interest

> Ample blood supply is the first principle of physiological efficiency The most potent cause of relative visceral ischæmia is cortico-thalamic in origin through activity of the sympathetic nervous system. In defence emotions, selective and purposeful stimuli inhibit the circulation of viscera not concerned with defence, but augment the circulation in organs and structures responsible for maximum effort in combat or escape[1] This selective activity of the sympathetic nervous
> may account for the injured trophoblast or the
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> ations upon uterine behaviour under the influence of
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> Associated with these were evidences during labour
> tive ischæmia diagnosed on the basis of Lewis's
> ns.[2] The appearance of anoxæmia of the infants at
> without reason to suspect intracranial pressure or
> narcosis as a cause

nd other observations prompted the initiation
amme designed to enhance the visceral blood
There were three simple approaches to this

breathing to develop maximum habitual intake
(Not one woman in a hundred breathes properly)
udes adoption of good posture and carriage

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[1] W Origin and Nature of the Emotions. London and
adelphia, 1915.
[2] T *Arch. intern Med* 1932 49, 713
Read G Revelation of Childbirth London, 1942.

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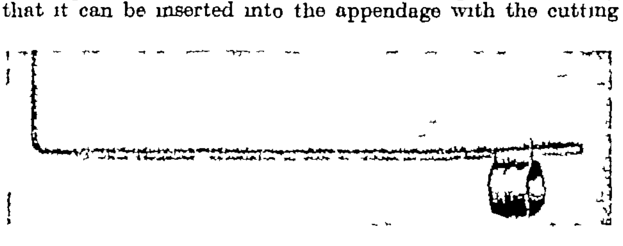

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J F TUTHILL

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[1] ner 1954 172 307

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> Ample blood-supply is the first principle of physiological efficiency The most potent cause of relative visceral ischæmia is cortico thalamic in origin through activity of the sympathetic nervous system. In defence emotions, selective and purposeful stimuli inhibit the circulation of viscera not concerned with defence, but augment the circulation in organs and structures responsible for maximum effort in combat or escape.[1] This selective activity of the sympathetic nervous system may account for the injured trophoblast or the ischæmic decidua before hypertension is established.
>
> Observations upon uterine behaviour under the influence of emotional stress disclose a high incidence of dysfunction of all types. Associated with these were evidences during labour of a relative ischæmia diagnosed on the basis of Lewis's observations.[2] The appearance of anoxæmia of the infants at birth was without reason to suspect intracranial pressure or maternal narcosis as a cause

These and other observations prompted the initiation of a programme designed to enhance the visceral blood supply[3] There were three simple approaches to this objective

(1) Correct breathing to develop maximum habitual intake of oxygen (Not one woman in a hundred breathes properly) This includes adoption of good posture and carriage.

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1 Crile G W Origin and Nature of the Emotions London and Philadelphia, 1915
2 Lewis, T Arch intern. Med 1932, 49, 713
3 Dick Read G Revelation of Childbirth. London, 1942

(2) Tensing and relaxing muscles performed without violence or exaggeration This is known to increase the surge of blood through muscles, and its influence upon the digestion and the bowels strongly suggests some form of visceral activity resulted from these exercises

(3) Elementary education in the changes and events of pregnancy and parturition, giving confidence and removing most, if not all, anxiety about childbirth This resulted in general and physical improvement and, by allaying of fears, minimised the constrictor influence of the sympathetic upon the visceral blood vessels

The value of such measures cannot be estimated with the certainty of laboratory experiments, for obviously they may be associated with a variety of causes and effects Toxæmia and pre eclamptic symptoms rarely develop under this régime sufficiently to demand active interference No absolute conclusion can be drawn from these observations but they may emphasise the possibility of a multiple or general origin of toxæmia as opposed to a primary visceral or focal cause

A woman of 27, who lost 3 babies between twelve and twenty weeks gestation with marked hypertensive pre-eclamptic symptoms, started this régime in part before her fourth pregnancy, and with the exception of limb moving exercises the whole programme was adopted soon after she missed a period Her diastolic blood pressure had remained around 80 mm Hg, and there was a faint cloud of albumin but no casts in the urine She was on a minimal NaCl diet and all went well until the thirty fourth week when albumin and blood pressure increased and some œdema appeared On admission to hospital she was treated with confident, companionable encouragement and reassurance and started to improve at once with no other treatment At thirty seven weeks she came into labour spontaneously and was delivered calm and relaxed without drugs, analgesics, or episiotomy She stated she had no discomfort that needed analgesia and refused it when offered She watched her 4 lb baby born, it was a toxic premature type, but owing to the nature of her labour cried lustily immediately and adjusted its general metabolism without difficulty I was fortunate in obtaining, with her consent, a colour film of her labour and delivery, and her breast fed baby of three weeks old This was one of several toxæmias of varying intensity which reacted in this way to the same procedures

Later I was travelling in South, Central, and East Africa studying childbirth in the tribes uninfluenced by modern science or European interference In the two hundred odd tribes and subtribes of whom I obtained information, I observed that the posture and carriage of women ensures breathing far more efficient than in cultural societies Relaxation and muscle tension are natural to their way of life They have no fear of childbirth but welcome pregnancy as a gift from their spiritual ancestors and labour as a joyous achievement though sometimes hard work Most of them are instructed in childbirth by experienced women teachers who assist and never leave them during labour Except for one or two quite degenerate tribes and others who had become urbanised by association with Europeans, the African woman appeared to me to be an excellent example of all I had taught as a means of avoiding dysfunction in pregnancy and childbirth

Amongst the African women eclampsia is extremely rare and in some of the Central Congo tribes we found it had never been known to occur This was equally true at all altitudes and amongst the badly and the well nourished people, the vegetarians, blood drinkers, and mixed food eaters It applied in the same measure to Bantu, Hamitic, Nilotic, and mixed races who live tribal lives in remote areas where the white man does not live or rarely visits

I offer these observations, Sir, as an appreciation of the clinical importance of the work of Dr Morris and his colleagues upon the circulation of the blood in the wall of the pregnant uterus, but I believe that the final the problem of toxæmia of pregnancy, as well tion of the uterus, will only be found by the coordination of all branches of science in the study human faculty and function

Petersfield Hants GRANTLY DICK REA

## COLD BATHS

SIR,—At this school cold baths have up till now compulsory every morning of the year It has suggested that this practice should be changed, an the course of discussion an important point has a on which we felt that it would be wisest to tak impartial outside opinion We wondered whether of your readers could suggest, roughly, what woul a suitable lower air-temperature in the bathroom (T are no considerations of heat or draughts to be t into account ) Perhaps this lower limit we are lookin might be defined as the point when the various risks exposure and the unpleasant shock begin to outweig "healthiness" and the power of waking one up th claimed for them

Bedales School
Petersfield Hants JOHN VINCE

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# Obituary

## HENRY WADE

Kt, C M G, D S O, M D Edin, F R.C S E

Sir Henry Wade, past president of the Royal C of Surgeons of Edinburgh and an honorary fellow o English, American, Australasian, and Irish Colleges, in his Edinburgh home on Feb 21, at the age of 78

A son of the Rev George Wade of Falkirk, he educated in Edinburgh at the Royal High School the university, where he graduated M B with first honours in 1898 The following year the South A war broke out and it was not long before his adven some spirit prompted him to volunteer for active se as a civil surgeon attached to the British Field F After eighteen months, the last eight of which spent in sole charge of the surgical beds in a military hospital in Pretoria, he returned to Edinburgh where for a year he was demonstrator in anatomy at the university At this point, however, he broke with tradition, in that when appointed as clinical tutor to F M Caird, then regius professor of clinical surgery, he forsook anatomy to study pathology, believing that a wide knowledge of this subject was of paramount importance to a surgeon Such was his reputation as a pathologist, that when he was elected to the fellowship of the Royal College of Surgeons of Edinburgh in 1903, he was appointed conservator of the college museum the same year, he continued in this office for seventeen y He began his pathological researches by stud the ætiology of carcinoma, and he published se papers on this subject in our columns in 1904 In he was awarded a gold medal for his M D thesis on t tive sarcoma of the dog In 1906 he tempor resigned from clinical work on his appointmen assistant pathologist to the Royal Infirmary, and fo next two years he performed the post-mortem exan tions on virtually all cases sent from the surgical w of the hospital

Wade was appointed assistant surgeon to Hospital in 1908 and to the Royal Infirmary in At this time the extramural school was flourishing, from 1906 onwards he was for many years muc demand as a lecturer in surgery and surgical patho both to students and to postgraduates Graduall interest in the pathological and clinical aspects of ur gan to transcend all others, though he always stoutly aintained that he was first and foremost a general rgeon. In 1913 he published his classical paper on the thological changes of prostatism illustrating his argu ents with many whole sections taken from blocks of e entire gland with the surrounding tissues. This rk helped materially to advance the surgical treatment all forms of prostatic disease and many of his ustrations were later used by his friend Hugh ung of Baltimore in his monumental textbook of logy

On the outbreak of war in 1914 Wade took command a captain, of the Scottish Horse Mounted Brigade d ambulance, to which he attracted many of his dents. Later, at Suvla Bay in Gallipoli his ' shell e" operating theatre close to the front line became ndary among the troops. In 1916 he was appointed sulting surgeon to the Egyptian Expeditionary Forces manded by General Allenby In recognition of his standing services in the field he was twice mentioned despatches, promoted to full colonel and appointed in 1918 and C.M.G. in 1919

Returning to Edinburgh in 1919 he quickly took up reins again and in 1924 he was promoted to the staff of the Royal Infirmary as surgeon in ordinary n before this he had gained an international reputa , and many visitors from all over the world went to his work He continued with research now more g clinical lines, and published many papers of practical portance to the advancement of urological surgery, uding some on vesical exclusion and ureteral plantation.

He retired from the Infirmary in 1939 at the end of statutory period of fifteen years service but yet ther war brought him immediately back into harness for the next five years he continued in active practice consulting surgeon to Bangour E.M.S. Hospital. e his administrative and organising genius was of reatest value to the hospital and to the Department Health

n the '30s Wade travelled widely, at the invitation of ical societies and colleges as lecturer and as official resentative of the Edinburgh college He was awarded honorary fellowship of the American College of eons in 1930 the Australasian college in 1935, the college in 1936, and the English college in 1943 was created a knight in 1946 On Dec 10, 1953 a r was given in his honour by the president and cil of his own college in recognition of fifty years of ice in office Besides acting on many committees subcommittees and as an ambassador for the college ome and abroad, he was a member of the president's cil from 1925 onwards he was president from 1935 37 and from 1943 to 1953 he was the representative the General Medical Council. When he retired the ident of the Council wrote of these ten years

Sir Henry Wade rendered notable service on the education mittee when the revision of the curriculum was under y and on the Executive Committee and in the ionary business of the Council his cautious judgment of great assistance His colleagues will long remember ntured comments on matters both educational and moral happy social interests and attractions and his unfailing e of humour

R L S to whom we are indebted for this record of de's career writes in conclusion :

"A fervent lowland Scot and always an individualist in ught and deed, he conformed to no pattern provided by seniors. He drove himself hard throughout his working and though he had a reputation for some measure of ability yet at heart he was the kindliest of men always ing and ready to help and advise his juniors He set the est standards for himself in his work and truly earned right to be considered as the father and leader of modern tural surgery in Scotland

Sir Henry was not an active sportsman but found an let for his energetic spirit in travel and latterly in horti ture He was a man with green fingers, and the garden his lovely 17th-century mansion house of Pilmuir became of the show places of East Lothian. An ardent student literature and verse he could recite at length from the ks of the national bard of Scotland, while his knowledge of medical, political and military history was profound. His life and work will long remain a stimulating memory

In 1924 he married Marjorie Fraser-Tytler, of Woodhouselee, Midlothian She died in 1929

## CECIL JOHN ALEXANDER WOODSIDE

### M.B Belf., F R.C.S I

Mr C J A Woodside, senior surgeon to the Royal Victoria Hospital, Belfast, died at his home on Feb 14

He was educated at Ballymena Academy, and at Campbell College and Queen's University, Belfast In 1917 after graduating M.B with first-class honours, he volunteered for the R.A.M C and served in East Africa till 1919 After demobilisation he held house-appointments at the Royal Victoria Hospital, later becoming surgical tutor and surgical registrar In 1921 he was appointed demonstrator in anatomy at Queen's University and later he served as a surgical specialist to the Ministry of Pensions and as resident medical officer in the Ulster Volunteer Force Hospitals in Belfast. He took his F R.C.S I in 1925 and the same year he became assistant lecturer in operative surgery in Queen's University—a post which he held until 1928, when he was appointed lecturer in surgical anatomy In 1933 he joined the staff of the Royal Victoria Hospital From its inception in 1948 he served with the Northern Ireland Hospitals Authority and he put in a great deal of the groundwork in the early days of the health service. His hospital work was not confined to the wards He took a wide interest in the conditions of the staff, and during the late war he was chairman of a ministry commission on the conditions and pay of the nursing profession in Northern Ireland

W S B writes Though Woodside was a general surgeon his main interest centred in urology on which his opinion was widely sought He was also a dexterous surgeon in all abdominal work, of which he did a great deal

He had little leisure, but he was interested in literature and in modern art, particularly industrial design He was also an expert and keen gardener In earlier years he used to sail on Belfast Lough In many ways he was a retiring man, but he was a good friend to those who had the fortune to know him well He will long be remembered by many generations of students whom he taught at all stages of their university career and by the nursing staffs on whose behalf he did so much good work '

## GREER EDMUND MALCOMSON

### M.D Lond., M R C.P

Lieut.-Colonel Greer Edmund Malcomson, who for many years held the chair of medicine in the University of Madras died on Jan 24 at the age of 76

The fifth son of James Malcomson of Belfast, he belonged to a well known Irish Quaker family He was educated at Bootham School, York, Owens College, Manchester and Guy's Hospital After graduating M B in 1902 he held house-appointments at Guy's, and he took the M.D degree as well as the D P H before joining the I M.S He served chiefly on the North West Frontier and later was seconded for service in Hong Kong While there he retired from the I M.S on his appointment as professor of physiology in the New University but he rejoined the Service in 1915, and was posted to the gruelling campaign in Mesopotamia.

In 1919 he returned to India and later transferred to the civil side of the I.M.S., when he was appointed physician to the government of Madras and professor of medicine with beds in the government general hospital In 1924 the sight of both his eyes was seriously affected by bilateral paracentral choroiditis, and he came home on sick leave but the lesions cleared up, leaving him with useful vision in both eyes and he was able to return to his duties in India. While in Madras he acquired a great reputation as a physician and established a large civil consulting practice During study leave in 1927 he obtained the M R.C P

After his retirement in 1931 he worked at King's College London helping Prof R J S McDowall in the preparation of his book, *Control of the Circulation of the Blood*. He checked with meticulous care the 7000 references which appear in the book After this he undertook research

R A G writes "Malcomson—Malky to his friends—was endowed with a charming personality He had a quiet, modest, and unassuming nature, and was beloved by his many friends He was deservedly respected and revered by his students and patients, many of whom continued to consult him after his retirement, some even making the journey from India When I visited India four years ago, I was impressed by the enthusiasm shown in many places whenever his name was mentioned, especially in Madras, where his skill and kindness are well remembered"

In 1906 he married Ida Mott, who had trained as a nurse at Guy's Hospital, and she survives him

### Sir CHARLES MARTIN

L W H writes "In your obituary of Charles Martin various tributes are paid to his independence of thought, which the following anecdote supports from another angle

"In 1905 on his journey to India, I was a fellow passenger on S S *Caledonia* and there was also a team of Sandow demonstrators going to demonstrate the virtues of physical culture In some deck sports, organised to vary the monotony, was a tug of war, four a side, and a team consisting of Martin, *two Indian Army officers, and myself was drawn against four* of the Sandow people Talking to Martin the evening before the event, I said I supposed those Sandow fellows would haul us round the deck Martin said in effect 'Not at all, brain can prevail over brawn, all we have to do is to use our weight' Next day he was proved right I sat, or rather leaned, tight at the end of the rope and felt the strain to be critical for less than a minute, then it was we who hauled the other fellows They *were* annoyed"

## Appointments

DE SARAM, PHYLLIS M M B Lond F F A R C S D A part time consultant anæsthetist Hampstead General Hospital

FEARNLEY, G R M D Lond M R C P consultant physician North Gloucestershire clinical area

JONES F R, M R C S, D P M asst psychiatrist, Mendip Hospital Wells

McGOVERN JAMES M B Glasg D P H M O H, Thornaby on Tees and Stokesley, and asst county M O Yorkshire

STEPHENS L S, M B Birm D OBST D P H asst. county M O H Worcestershire and M O H, Droitwich borough and Droitwich and *Martley rural districts*

**Manchester Regional Hospital Board:**

- CASHMORE A A M D Lond whole time child psychiatrist Booth Hall Hospital
- FOX D L M B Manc D P M whole time asst psychiatrist Lancaster Moor Hospital
- HERBERT F J M D Glasg F R F P S whole time consultant physician in geriatrics Blackburn and district hospitals
- HEFFERNAN H I, L R C P I D A whole time asst anæsthetist, Ashton Hyde and Glossop hospitals
- O'HARE, BERNARD M B N U I D M R D whole time asst. radiologist, Bolton and district hospitals

**Colonial Medical Service**

- DALY W M K M B N U I M O Uganda
- DOWNES, P W E M B Brist M O South Pacific health service Fiji
- FIELD, CONSTANCE E M D Lond, M R C P pædiatric specialist Singapore
- GANGULI P K, M B Calcutta D M R D radiologist Trinidad
- HACKETT E W R, M B Dubl D L O senior specialist Federation of Nigeria
- HUMBY T G M R C S medical superintendent Barbados
- LATHAM M C M B Dubl M O Tanganyika
- MACKINNON ANNE E C M B Glasg D OBST M O, northern region Nigeria
- MAJEKODUNMI M A M D Dubl, M R C P I, D C H senior specialist Federation of Nigeria
- MANEY W A W F R C S I F R I P S surgical registrar (orthopædic) Singapore
- SERLE WILLIAM O B E M B Edin D T M & H D P H P M O Southern Cameroons Federation of Nigeria
- TRANTER A W M B Lond D C H M O, Tanganyika
- TREDWAY C C M B M O Kenya
- WYDELL I H M B M O Tanganyika
- WYNTER WEDDERBURN L F M B M R C P D C H medical specialist (pædiatrics) Jamaica
- YOUNG K D M R C S medical superintendent, Hargeisa Group Hospital Somaliland Protectorate
- YOUNGLAO L P M B N U I D T M & H M P H D D M S, Trinidad

Dr James Hunter whose appointment as M O in Tanganyika was announced in our issue of Jan 15 has now declined the post

## Births, Marriages, and Deaths

### DEATHS

[illegible] On Feb 19 at Rivermead Rickmansworth Herts [illegible]el Nuttall M D Lond aged 85

## Diary of the Week

MARCH 7 TO 12

### Monday, 7th

POSTGRADUATE MEDICAL SCHOOL OF LONDON Ducane Road, W
4 P M Prof Melville Arnott Fever in Disease

HARVEIAN SOCIETY
8 15 P M (Royal College of Surgeons Lincoln's Inn Fi
W C 2) Prof Clarence Crafoord (Stockholm) In
auricular Septal Defects

### Tuesday, 8th

UNIVERSITY OF LONDON
5 30 P M (Westminster Medical School Horseferry Road S.W.
Academician W A Engelhardt (Moscow) Mech
chemistry of Muscle (First of two lectures)

ROYAL SOCIETY OF MEDICINE 1, Wimpole Street, W 1
5 30 P M *Experimental Medicine and Therapeutics* Mr J
Aylwin Dr Denys Jennings, Dr A C Da
Mechanisms at the Lower End of the Œsophagus
8 P M *Psychiatry* Prof A Querido The Amsterdam P
chiatric First aid Scheme and some Proposals for
Legislation

ST MARY'S HOSPITAL MEDICAL SCHOOL, Paddington W 2
5 P.M Dr James Walker Postmaturity and Fœtal Anox

INSTITUTE OF DERMATOLOGY, St John's Hospital, Lisle Str
W C 2
5 30 P M Dr Phyllis Wade Radiotherapy of Skin Can
(First of two lectures)

CHELSEA CLINICAL SOCIETY
8 30 P M (Rembrandt Hotel, Thurloe Place, S W 7) The B
of Coventry Dr Ernest Claxton Divine Healing and
Medical Profession

UNIVERSITY OF BRISTOL, Bristol, 8
8 30 P M Mr R Scott Stevenson The New Outlook
Otolaryngology (Patrick Watson Williams lecture.)

MANCHESTER MEDICAL SOCIETY
8 P M (Medical School) *Surgery* Mr Ambrose Jolleys Su
of the Newborn

### Wednesday, 9th

UNIVERSITY COLLEGE, Gower Street, W C 1
5 30 P M Dr C R Skoglund (Stockholm) Functional Orga
tion of Spinal Interneurones (First of two lectures)

ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE, 28, Port
Place, W 1
3 30 P M Dr Dorothy Makepeace Medical Aspects of Child C

INSTITUTE OF DERMATOLOGY
5 30 P.M Dr R W Riddell Mycotic Infections of Subcuta
Tissues

INSTITUTE OF LARYNGOLOGY AND OTOLOGY 330, Gray's Inn R
W C 1
5 30 P M Dr Imrich Friedmann *Otitis Media—Experim*
and Human

UNIVERSITY OF OXFORD
5 P M (Radcliffe Infirmary) Prof C A Wells Experim
Approach to Surgical Problems (Litchfield lecture.)

MANCHESTER MEDICAL SOCIETY
4 30 P.M *Pathology* Dr D G Evans Study of Anthrax

### Thursday, 10th

ROYAL COLLEGE OF SURGEONS OF ENGLAND
5 P M Prof Gilbert Causey Place of the Vascular Supply
Fatigue and Regeneration of Peripheral Nerve (Hunter
lecture.)

UNIVERSITY OF LONDON Senate House, W C 1
5 30 P M Prof P Karrer (Zürich) Curare Alkaloids. (F
of two lectures)

INSTITUTE OF DERMATOLOGY
5 30 P M Dr Wade Radiotherapy of Skin Cancers (Sec
of two lectures)

LIVERPOOL MEDICAL INSTITUTION, 114 Mount Pleasant Liverp
8 P M Mr Donald Young Surgical Aspects of Male Inferti
Mr F C Dwyer Suppurative Arthritis of the Hip-
in Childhood

UNIVERSITY OF ST ANDREWS Medical School Small's Wynd Du
5 P M Dr W C Swanson Review of Carcinoma of the Br
in the Eastern Region

### Friday, 11th

UNIVERSITY OF LONDON Senate House W C 1
5 30 P M Professor Karrer Curare Alkaloids (Second of t
lectures)

UNIVERSITY COLLEGE
5 30 P M Dr Skoglund Functional Organisation of Spi
Interneurones (Second of two lectures)

POSTGRADUATE MEDICAL SCHOOL OF LONDON
4 P M Dr Wilfrid Oakley Peripheral Vascular Disease

ROYAL COLLEGE OF SURGEONS OF ENGLAND
5 P M Mr D S Poole Wilson Tumours of the Bladder

INSTITUTE OF DERMATOLOGY
5 30 P.M Dr Brian Russell Benign Tumours of the Skin

INSTITUTE OF LARYNGOLOGY AND OTOLOGY
3 30 P M Dr Friedmann Basis of Chemotherapy in E
Disease

ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASG
242 St Vincent Street
5 P.M Dr Thomas Anderson Antibiotics

# Notes and News

## MUSIC FOR THE MENTAL PATIENT

sic evokes such diverse and inexplicable responses from entally sound that few would feel justified in predicting fects on the mentally sick Yet from ancient times has been prescribed therapeutically and considerable its from its use have been recorded Mr Frank Howes, critic of the *Times* in a Cantor lecture to the Royal ty of Arts on Feb 21 recalled some of those occasions when David played before Saul, Galen prescribed music ake-bite and Farinelli sang to Philip V of Spain But more interested in modern musical prescriptions, and es in a workmanlike manner the question: "What sort tients, suffering from what sort of diseases, can be healed hat sort of music?"

e mere formulation of the question as he points out, s that it cannot be settled by scientific method: there oo many variables That it has some effects—occasion violent effects—is undisputed but those who use it enthusiastically are not necessarily those who have led them most closely Dr Licht in his book *Music in cine*, advocates light music and plenty of it plainly ing his conviction that "bad music is better than good hospital purposes. For patients with arteriosclerotic hosis he prescribes old time favourites played softly for ral periods daily" But this is in America; those who nge gramophone recitals and concerts for English mental ents do not find Mr Howes said that the endless repeti n of old favourites is at all appreciated They agree that e familiar airs in the programme are desirable enabling patients to accept unfamiliar items more readily but y also find as might be expected that mental patients not listen for very long because their attention is less sistent than that of normal people and they cannot attend n for a short time to anything too complex because their wers of concentration are poor

The late Dr Mitchell a member of the Council for sic in Hospitals made some controlled experiments at dingham Park Hospital and these have been continued d extended by Dr A. Zanker Dr E Cunningham Dax h made a study at one time in which music was combined th graphic art: he played music to a group of patients d asked them to paint their impressions. The pictures erally showed either depression or elation Mahler's [illegible] released in one patient so much despair that he ng his picture from him and rushed from the room whereas itten's *Variations on a Theme of Purcell* produced general tion. Perhaps the most remarkable result was that proed by Mendelssohn's *Overture to a Midsummer Night's eam* 13 patients out of 17 painted scenes of violence robberies, fires, a train accident a ship in a storm a war e a murder and a suicide How surprised Mendelssohn uld have been.

The gramophone record, which allows of repetition and minates fluctuations in performance is a useful piece of quipment for those studying the effects of music and has abled them to classify listeners into types. Mr Howes self favours four types but for the purposes of medicine says, three will do: Cecilians, who are susceptible to pure und; Dionysiacs, in whom the response is emotional; and Apollonians, the "purely musical" Roughly this means at the response to music is a sensuous, an emotional or an tellectual experience In hospitals it is the emotional ponse that matters, for the release of emotional material y the music may relieve the patient and make him more cessible to psychotherapy As Dr Mitchell put it: "In sychotherapy emotional experiences are of primary import ce and it was these rather than conscious intellectual ressions, that we wished to foster in talking with patients on the music they had heard."

As Mr Howes admits, musical therapy is still largely pirical in its methods and incalculable in its results; but is none the worse, he thinks for that Medicine like music is art and both are recalcitrant to scientific method

## AIDS FOR THE DISABLED

Of all the consequences of physical disability loss of dependence is often the most feared and resented To offer disabled person a helping hand is—as we are sometimes cutely aware—to remind him yet again of his misfortune; hence the fullest advantage must always be taken of those devices which help to promote a sense of self reliance With this in mind the British Red Cross Society held last week at their London headquarters an exhibition designed to illustrate the large variety of inexpensive but effective aids now available for use by the disabled Many of these are so simple that they can readily be constructed at home yet their value to patients is often incalculable Especially will women afflicted with severe arthritis welcome any device that enables them to perform their own toilet and the exhibition included many such appliances, ranging from long handled combs toothbrushes, and lipsticks (for those unable to raise their arms) to a remarkably effective "stocking puller on" (for patients with limited flexion of the spine) Among the most exasperating of minor disabilities is that involving a defective grip yet this may often be overcome by the simple expedient of padding the handles of implements with cotton wool and binding them firmly with adhesive tape and a corrugated rubber mitten enables these same patients to carry out easily the otherwise temper trying process of turning door handles.

One armed patients usually acquire remarkable dexterity in the other limb but there remain many activities which their disability must render difficult or impossible Aids for such patients include a useful universal tool (somewhat similar to those comprehensive implements beloved of schoolboys) a playing card holder and a highly ingenious knitting machine For armless or paralysed patients several firms now produce electrical devices which when a knob is pressed with the chin turn over the pages of a book; one of the models on show combines such a device with an apparatus which projects a picture of the page on to a nearby screen—an arrangement of obvious value to invalids unable to sit up

Thanks to the new materials now available (in particular the plastics and light alloys) almost all these devices are not only functionally efficient but pleasant to look at—an aspect which disabled people are often specially quick to appreciate

## AN UNBREAKABLE SYRINGE

THE advantages of an unbreakable syringe are obvious The 'Atlas' syringe which is made of translucent nylon is a considerable step forward in this direction Its barrel and nozzle are in one piece and the interchangeable plunger fits loosely in the barrel being rendered leak proof by an elastic piston ring fitted very close to the end of the plunger This syringe gave better results under vacuum than any more conventional syringe tested The plunger is hollow and the handle can be unscrewed so that spare needles, &c., can be accommodated inside it The eccentric nozzle is so constructed that if a Luer mount is required one simply cuts off the Record extension of the Luer mount. The makers claim that this syringe withstands boiling water indefinitely and autoclaving at 120°C but presumably 160 C in the hot-air oven would damage it Prolonged immersion in solutions of phenol or its derivatives may be harmful Although the makers say that the absence of soldered parts eliminates crevices in which matter can lodge the piston ring groove in the plunger is just such a crevice; but this ring is easily removed for cleaning The graduations are moulded on the surface of the barrel and should therefore be permanent and the whole assembly is remarkably light Provided that it does not become opaque with use this syringe should prove an advance on older types—although many would no doubt prefer one that can be dry-sterilised at 160 C. The distributors are Messrs Chas F Thackray Ltd 10 Park Street Leeds 1 Prices range from 9s 6d for the 3 ml. size to 15s for the 20 ml size.

## FOOD FOR SICK CHILDREN

THE proper feeding of sick children is often a worry to the doctor especially when the child is nursed at home So the second edition of Great Ormond Street's concise guide[1] is likely to have a wide appeal It gives useful general advice on the selection and serving of food for children and diets for fevers convalescence postoperative needs (including tonsillectomy) nephritis diabetes, and obesity Of the 15 pages 3 are devoted to gluten free diets for use in cœliac disease The need for additional protein in long-continued fevers and after trauma is properly stressed On the other hand there are points at which the booklet seems to be open to criticism. The revision of the text has perhaps been over hasty for the section on diabetic diets still refers to the child's "rations." (Incidentally the diabetic diet appears to be planned on the outmoded principle of observing carbohydrate protein fat ratios ) Again was it necessary to retain a ketogenic diet ? And it is perhaps a pity that only one proprietary brand of milk products should be recommended when others equally good are on the market

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[1] Diets for Sick Children. 2nd ed. Hospital for Sick Children Great Ormond Street London. W C.1 1954 Pp 15 1s.

### DOCTOR IN CAPTIVITY

Colonel K P MacKenzie, who had served in the R A.M C since 1914, was A D M S of the 17th Indian Division when he was captured by the Japanese at the Sittang bridge in Burma, in February, 1942 He spent a few months in Moulmein jail and was then transferred to Rangoon jail, where he was the senior medical officer until his release nearly three years later His account [1] of the conditions which he and his fellow prisoners endured in Japanese hands—overcrowding, long stretches of solitary confinement, inadequate food and water, rudimentary medical supplies and sanitary facilities, and the sufferings imposed by the arrogance and insensate sadism of their captors—makes grim reading, but is inspiring in its unemphatic portrayal of the quiet heroism of British officers and men under physical and mental stresses almost unendurable even to read about This book, which is claimed to be the first about the late war by a serving medical officer, should hearten any young doctor who doubts the usefulness and scope of a medical career in the Forces

### ELIZABETH TUDOR

Sir Arthur MacNalty has written an authoritative biography of Queen Elizabeth I,[2] in which he includes medical details—though these are few compared with those in his previous biography of Henry VIII Medical readers will be particularly interested in the chapter on " the Queen's medical case sheet " and in the short biographical notes on fourteen of her physicians There is also a list of twenty kings, princes, and noblemen whose suits for the Queen were seriously put forward and considered Queen Elizabeth was subject to attacks of migraine from childhood In 1553, at the age of 20, she had an illness which seems to have been scarlet fever, and which left her with acute nephritis This troubled her for about two years, but did not prevent her from being imprisoned in the Tower She recovered completely and never showed symptoms of the chronic form of the disease She developed smallpox in 1562 and " was all but gone " She had chickenpox in 1572 and whooping cough in 1580 In 1569 she had an open ulcer above the ankle which prevented her from walking The French Ambassador said she would not live long, and the future King Henri IV told his mother that he would not consider marrying her, because " she was not only an old creature, but had a sore leg " The ulcer seems to have lasted about nine years She also had attacks of " the Mother "—a term used for hysterical fits " because it seizeth upon women, though men too, have something like it " On one occasion she was " for four hours speechless, and as if dead in a swoon " She was short-sighted and suffered from indigestion, toothache, and pelvic disorders Her final illness in 1602 was probably a streptococcal infection of the throat, but the information is scanty

## University of Cambridge

On Feb 19 the following degrees were conferred

*M B , B Chir* —D M Surrey Dane
*M B* —W S Ogden

Dr R N Salaman, F.R S , has been elected to an honorary fellowship of Trinity Hall

## University of Hull

On July 19 the honorary degree of D.SC will be conferred on Lord Adrian, O M , P.R S

## Nutrition Society

On Saturday, March 12, at 10 45 P M , at St Mary's Hospital Medical School, London, W 2, Dr H E Magee will take the chair at a symposium on Alcohol and its Nutritional Significance The speakers will include Prof E M Jellinek, Dr J Trémolières, Dr E Le Breton, Dr L Dontcheff, Dr Miles Weatherall Dr H. M Sinclair, Prof B S Platt, and Mr A W Wilkinson

## British Congress of Obstetrics and Gynæcology

Applications for membership of this congress, which is to b held in Oxford from July 27 to 30, should be sent withou delay to the hon secretaries, Radcliffe Infirmary, Oxford

## European Hæmatological Society

The fifth congress of this society will be held in Freibur im Breisgau from Sept 20 to 25 Further particulars may b had from Dr A Piney, 152, Harley Street, London, W 1

## Institute of Dermatology

The sixth of a series of semi permanent exhibitions being held at the Institute, Lisle Street, London, W C.2, fro March 4 to 25 It has been arranged by Dr H. Haber an is on Benign Tumours of the Skin

## International Fertility Association

The Second World Congress on Fertility and Sterili will be held from May 18 to 26, 1956, in Naples Furth particulars may be had from Dr G I M. Swyer, Obstetr Hospital, University College Hospital, Huntley Street, W C

## Institute of Psychiatry, London

On Thursday, April 14, at 5 30 P M , at the Maud Hospital, Denmark Hill, S E 5, Prof H McIlwain will gi a lecture on Maudsley, Mott, and Mann on the Chem Physiology and Pathology of the Mind

## Postgraduate Course in Radiology and Radiotherapy

The Faculty of Radiologists will hold a postgraduate co in diagnostic radiology and radiotherapy at the Royal Col of Surgeons, London, W C 2, on Saturday and Sund March 19 and 20 Further particulars may be had from t secretary, 45, Lincoln's Inn Fields, London, W C 2

## Postgraduate Course at Cardiff

A course for general practitioners is to be held at Cardiff Royal Infirmary and Llandough Hospital from April to May 7 Further particulars may be had from the secret Welsh National School of Medicine, 34, Newport Ro Cardiff

## C M F /M E F Army Physician's Reunion

The tenth annual dinner will be held at Simpson's in-t Strand, London, W C 2, on Saturday, April 2 Furt particulars can be had from the hon secretary, Dr A Wille 59, Harley Street, W 1

## South West Metropolitan Region

A chest diseases group has been formed in the eastern a of this region, under the presidency of Dr W J Gill The fi clinical meeting of the group will be held at St James' Hospi Ouseley Road, Balham, S W 12, on Saturday, April 23, 2 30 P M , when the speaker will be Sir Clement Price Thom Further details may be had from the hon. secretary, D G C Taylor, 27, Queen Anne Street, W 1

## International Society for the Study of Biologi Rhythm

This society is to hold a conference from Sept. 15 to 17 Stockholm The subjects chosen for discussion are Rhyth mical Phenomena in the Nervous System, Cybernetics, a Rhythm and Industrial Medicine Further particulars m be had from Prof Ture Petrén, Karolinska Institut Stockholm 60, Sweden

## Travelling Fellowships in Ophthalmology and Otolo

The Medical Research Council invite applications f Alexander Pigott Werner travelling fellowships in ophthalm logy and otology for 1955–56

These fellowships are intended for medical graduates who wish work in ophthalmology or otology at a centre abroad before takin up positions for higher teaching and research The fellowship provide a maintenance allowance at the rate of £650 per annum for a single fellow or £900 per annum for a married fellow A allowance is also made for travelling and other expenses For of application may be had from the secretary of the Counc 38 Old Queen Street London, S W 1, with whom applicatio must be lodged by March 31 1955

CORRIGENDUM *Post pregnancy Osteoporosis* —The sectio shown in figs 2 and 3 of the article by Dr B E. C. Nord and Mr A Roper (Feb 26, p 431) were stained by th picro Mallory method

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[1] Operation Rangoon Jail. By Colonel K. P MACKENZIE R.A.M C. retd. London Christopher Johnson 1954 Pp 201 15s.

[2] Elizabeth Tudor By Sir ARTHUR SALUSBURY MACNALTY, K.C B M Oxfd F.R.C.P , F R.C S London Christopher 1954, Pp 272 18s

# MENTAL HEALTH AND SPIRITUAL VALUES*

Sir GEOFFREY VICKERS
V C M.A.

ALL of us are heirs of two traditions which are hard reconcile, the scientific and the prescientific  Each s its own language and its own concepts and their plications seem partly inconsistent  so it is hard to anslate from one language to another or even to speak th conviction in either  Prophets philosophers and ets had been expressing their intuitions many centuries fore modern science was born, and they dyed our guage deeply with images and implications about the ature of man and his place in the universe which are eign to the images and implications of science  This mpers our talk and confuses our thought

During the last fifty years psychologists have added man's personality a new dimension in which much himself lies hidden  Sociologists and social anthropo gists have shown how deeply he is conditioned by the al nexus and have asked how far he can usefully be idered in abstraction from it  Anatomists and iologists have made him more conscious of the sical basis of mind, and now the physicists are ing them with exciting, if disturbing theories about working of the brain

These new insights clash with our older concepts out the nature of man  They illuminate but y also confuse  Prescientific language whether of tians or of humanists was not made to the sure of such a creature  and scientific language s not cover the whole of the ground  No wonder t of us find it difficult to say all we want to say about n on the basis of any one consistent assumption  It ot easy to see how a man can really be at one and the e time a soul accessible to Grace, a responsible moral g, an animal a machine a cell in an organic society a random unit which is only significant statistically in ordinary speech we are continually using words ch have all these implications  and if we did not e would be some things which we could not easily

If we have not yet resolved our contradictions of guage and concept we can at least refuse to believe t any language or any concept completely represents truth behind it  and when we are tempted to seek tisfaction of consistency by averting our eyes from e aspect of experience let us remember Walt itman's words :

> Do I contradict myself? Very well then I contradict
> self. I am large; I contain multitudes

* * *

The ancient controversy between believers in a God ntred world and believers in a man-centred world dates k before the birth of Christ and still divides Christian l humanist today  It involves the question whether itual values are rooted in the nature of things and have absolute validity for individual men or ther they are merely socially determined norms in other circumstances would be determined ently

en do in fact hold strong convictions about what uld be sought and avoided accepted or rejected ured or abhorred  Some may call these principles dards virtues; others may call them rationalisations eralisations abstractions from the stream of experi e. Yet though they would differ about the origin l validity of these evaluations they would not differ about their existence or their power to affect behaviour consistently and thus to give to the characters of men and nations such coherence and distinctiveness as they possess.

In the history of thought some of these evaluations have persistently been made and taught as claiming the acceptance of men not as being socially useful but as being the right response for an individual man to his nature and his situation  Some indeed are also socially useful and would probably be evolved by any successful social group but others are not so easily explained; and these curiously, are found in identical terms in cultures which are independent and diverse

Early in the first millenium before Christ, a little pastoral tribe on the sun bitten hills of Judæa produced a literature which is alive today  It has lived because its teachers were concerned not so much with social duties as with the preconditions of the good individual life

> ' Who shall ascend into the hill of the Lord?  Even he that hath clean hands and a pure heart  that hath not lifted up his mind unto vanity nor sworn to deceive his neighbour '

A little later in time and far removed in space the Indian prince Gautama was teaching the same attitude

> Whoso keeps his eyes from vanity  controlled and temperate faithful and strenuous Mara cannot overthrow
> Who speaks or acts with purified mind him happiness accompanies as his faithful shadow  They who have not lived purely in their youth, these ruefully ponder as old herons by a lake without fish

Yet a little later on the other side of the Aegean, Plato was describing in allegories which still move us the relation between the delusive world of sense and the eternal verities behind them the discipline of mind and body needed to apprehend truth goodness and beauty and its great reward

Jew, Indian and Greek had profoundly different ideas about the nature of the universe and about man's place in it but they shared an almost identical view about the route which a man must take to apprehend it or at least about the initial steps.  They are at one in stressing the need for the  purity  which comes from turning away from  vanity '  and purity and vanity mean, I think much the same to them all  They are extremely general concepts to be valued not so much for themselves but as the preconditions of apprehending other values  The Buddhist may live in the world but he must not become ' attached  to it  the Christian may live in the world but may not  lay up treasure ' in it.  The mind which is thus unattached is pure  " He who has no wound can handle poison  said the Buddha  Paul said " To the pure all things are pure '

To scientists of many disciplines from social anthropology to neurophysiology as well as to psychologists it must be a matter of great interest that a creature such as man has produced and nourished such an ideal as this.  It does not seem to be of a kind which societies would naturally evolve; indeed it has often produced conduct which society has rated as strongly antisocial It would not seem likely to survive  yet it has survived It originated with peoples two of which had no idea of rewards in an after life  and though the Buddha commended his  right path '  as a way of escape from the wearisome cycle of rebirth, he commended it also sometimes rapturously as the way to supreme satisfaction here and now  So did the others.  So do those who commend it today

Somewhat later again Jesus of Nazareth restated earlier Jewish insights in a much more positive and dynamic way  When he summed up " the law and the prophets '  within the commandment to love God and neighbour, he placed love in the forefront of spiritual values  and he exemplified his teaching by his life in a

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[illegible] from an address given at the World Congress for Mental Health at Toronto in August 1954 way which must stir the imagination of thoughtful men, whether Christian or not

“ Love ” and “ non attachment ” are opposite poles of the same magnet They involve a respect and a compassion for individual human beings as such and a corresponding lack of respect for their differing material circumstances They cannot safely be separated, though they often are They do not imply all the spiritual values but they provide the key to reconciling their eternal conflicts

For spiritual values are in constant tension They come into conflict wherever we reach the level of practical decision in concrete situations—and it is only at this level that spiritual values appear in action Our ideas of mercy and of justice, for example, affect our legal and our penal codes and the way in which these codes are applied in particular cases At these levels they encounter socially determined norms, with which they sometimes conflict and sometimes concur

In the practical decisions of life, spiritual and social values are always observed in action together and in their operation they overlap The Christian, however—and not the Christian alone—would assert that they are not identical and would appeal to history to show that our values are not derived solely from social convenience but are deeply affected by often conflicting insights derived from some other source

It is possible to find this other source simply in the predicament of individual man The history of man's thought, it may be said, is the record of his search for a way to organise his experience so as to make it significant or at least bearable to him Human self-consciousness and human memory give to each individual a sense of separateness, of continuity, and of purpose, which accord strangely with a creature so social, so transient, and so weak How should he bear either the burden of his separateness or his fear of losing it ? How prevent his desires from frustrating each other ? How support their frustration by event ? On what should he set his heart which will not let him down ? These questions, however unformulated, lie at the core of the experience of being human Spiritual values it may be said, are answers to this unspoken prayer They are ways of organising experience

This would not be accepted by any of the rival views as an adequate explanation of spiritual hunger , but all, I think, would agree that the hunger exists They would differ about its origin and its nature and would probably be unable to agree even on an appropriate name for it , but they would not differ about its existence Freud wrote

> “ I have no knowledge of having had in my early years any craving to help suffering humanity My innate sadistic disposition was not a very strong one, so that I had no need to develop this one of its derivatives ”

The Christian, who is first repelled by the implications of this passage and then puzzled to recall that Freud did in fact devote his life, with outstanding success, to healing the sick and indeed to casting out devils, may get some light by reading, a few sentences later “ In my youth I felt an overpowering *need* to understand something of the riddles of the world in which we live and perhaps even to contribute something to their solution ” Freud does not in this passage offer any psychological explanation for this “ overpowering need ” , and if he did, the need would remain a hunger

I want, then, so far as possible, to concentrate on the needs and the satisfactions which spiritual values are invoked to explain, without asserting or denying their rival explanations What we observe and experience is process—that is, happenings and the tendency for things to happen, including, in human behaviour, response and the te [illegible] to respond We can discriminate between [illegible] th great refinement and recognise in them common aspects , but we have an unhappy linguistic habit of labelling these aspects with abstract nouns—and I have a deep distrust of abstract nouns

The responses which spiritual values are invoked t explain have one striking feature in common The create far more problems than they settle To accept spiritual values does not take the tensions out of life While it resolves some, it creates many and heightens all What is claimed for it is that it supplies the vision an the strength to support them and to grow by them I is this which distinguishes the answer of religi in response to the perennial question of distracted humankind

* * *

What of the answer of psychology ? When I as myself and you “ What, if anything, has mental heal to do with spiritual values or they with mental health ? I mean, on the one hand, “ How far are spiritual valu insights into the conditions needed for mental health ? and, on the other, “ How far does our develop understanding of mental health and mental illness thr light on the meaning and nature and validity of spirit values ? Does it challenge or reinforce them ? Is th increasing knowledge likely to make for our spirit well being or for our spiritual decay or is it likely be as equivocal as other scientific knowledge has so f proved to be ? ”

These questions are highly topical The doctrine progress, after two centuries of phenomenal growth, on the defensive Its critics press two formidab attacks

They assert first that the growth of knowledge d not involve the growth of well being It does not ev give us greater control over our environment The id that it does so is based on the fallacy that the environme is finite, a continent of which the advancing frontier science leaves an ever smaller part unconquered Th say the critics, is an illusion , for we make our o environment as we go along Every act of so-call control lets loose a thousand new variables, which in th turn will demand to be known and controlled , and in t meantime these increase the factors to which we m respond and reduce our knowledge of them Thus t faster we change our environment, the less we know The frontier of control shrinks, as the frontier of pow widens , and it will go on shrinking, until we use o power not to change but to hold constant the limi tions within which we are content to live and develop

These voices were first heard when a century of relati peace broke in the thunderstorms of 1914 , and th used to draw their examples from the effect of science war From the aircraft to the hydrogen bomb there h been no lack of evidence that the power of science is least ambivalent Yet still there stood the belief that was a curse only when misused in war Men h unhappily progressed faster in physical than in soc knowhow They needed a few decades to catch up

The critics now press the attack on this inner strong hold Even power used peacefully and with good inte leads us into ecological traps from which we may or m not escape Go which way we will, we shall meet ou selves coming back Sir Macfarlane Burnet illustrat this in a recent address

> “ Urban life, a necessity for the development of civilisation inevitably led to the development of infectious disease the science of applied microbiology has liberated us from th ecological trap but led us into the other of over populati Birth control can save us from over population but confron us with the new trap of genetic deterioration Wherever utilise knowledge for the short-term satisfaction of our desi for comfort, security, or power, we are all too prone find that on the long term view we are creating one mo ecological trap, from which sooner or later we must extrica ourselves ”

is progress say the critics is like that of a tightrope lker who has tied the ends of his pole to the wire he lks on Every move to redress his balance is bound to turb it

The other line of attack is different Apostles of gress in the past have assumed that the behaviour of n and of societies is governed by laws like the laws of nce and that knowledge of these laws will give them ntrol of their individual and collective fate as great that which their physical knowledge was supposed to ve given them over Nature Neither assumption say e critics, is necessarily true and if the first were e the second would not follow The only result ich would logically follow would be a vast enlargement the possibilities of tyranny

We cannot decide this by an appeal to history for still know far less about the behaviour of men and tions than about the behaviour of atoms and nebulæ d what we know is of such relatively recent date that tory has not had time to condemn or approve the ect of this knowledge on our affairs It may be that wledge about ourselves will prove a less equivocal t than knowledge about the universe Can we hope t, however two-edged are the swords wielded by the er sciences mental science at least will set us no logical traps, that it will bring us not only knowledge wisdom ?

Descartes foresaw this question and made a tentative ly The flood of knowledge which would enable us make ourselves lords and masters of life would he ught, be useful not so much for the "invention of an inity of contrivances" as for the preservation of health anyone could make men *plus sages et plus habiles* it the doctors Thus he cast the medical profession nobly positive rôle If we make a realistic estimate hat might be achieved in the field of mental health far, if at all can we expect it to meet the critics of ress and justify the hopes of Descartes—to make r value judgments more noble more acute or at t more consistent ? To make men more sensible may a pedestrian ideal but it looks at least more hopeful n to make them still more clever

* * *

hy have we come to expect less of the doctors than Descartes ? Partly I suggest, because we stand at end of the hundred years which has seen the conquest bacterial infections This has been the outstanding ct of medicine on human life in the last ten decades d it has strongly affected our understanding of alth.

This achievement eliminated half a dozen lethal eases ; made possible aseptic surgery shaped the nt concept of public health and made possible the wth of cities It also fortified in the layman's mind ancient and I think mischievous idea that a disease an external entity an invader to be repelled and him to regard health negatively as the absence of ease

Experience if not wisdom may well lead us to revise e ideas The conquest of bacteria has not only raised expectation of life it has also raised the rate of ease of populations, the incidence of diseases which more slowly and the number and proportion of the d, especially the chronic sick We may be better f but we certainly set loose far more variables than we ained If the virus diseases should capitulate as the terial diseases have done this process will be still ther speeded

Thus already the attention of doctors and laymen ke is turning to two fields which have been relatively lected (1) to the possibility of building up health a kind which will carry a higher degree of general munity ; and (2) to the problem of bearing and lping each other to bear—not only stoically but fruitfully—the prolonged years of enfeeblement and degeneration which we have won by conquering pneumonia Both these problems are directed not to removing hazards but to making ourselves fit to bear them.

The emphasis in preventive medicine has shifted from the lowering of hazard to the raising of immunity , and in doing so it has shifted from things which can be done for people to things which people must do for themselves The change is significant it reverses a long accepted trend In equating himself with his environment, it has been the pride of progressive man to make his environment fit him To accept the environment and learn to be equal to it is by no means orthodox—but it is refreshingly sane ,

But there still lies far in the background the concept of health as a dynamic condition, of which immunity to disease is only one reflection Our knowledge of constitutional types is still slight still slighter is our knowledge of what determines the strange variations in apparent vitality between man and man or of how far this elusive quality can be developed Occasional innovators in teaching and training assert and demonstrate that we might make more of ourselves than in fact we do but by and large only the mountaineer and the athlete try to get fit rather than merely to keep well.

I venture on these speculations because I feel that we laymen dazzled by the results of defeating bacteria tend to think that the rôle of science is to remove hazards rather than to fit us to face them This I think is a dangerous fallacy I do not believe that it is true of physical science or even of medicine—except at a price which we should be unwilling to pay I am sure that it is not true of science in relation to mental health

* * *

The conquest of infection has had little effect on mental illness, except to remove from that category what had been regarded as a major psychosis—namely general paralysis of the insane Yet during the same period there has been a notable advance in the cure of mental illness and, I think in its prevention also New treatments have begun to make some impact on the major psychoses but I am chiefly concerned with the impact of new psychological and chemical knowledge on the more widespread conditions of neurosis and mental stress which are a characteristic of our age and a reproach to it

The main characteristic of mental ill health is inability to bear experience The condition which takes the distressed human being to the psychiatrist is fundamentally the same as that which takes him to the priest or to the philosopher, and it is legitimate and important to compare what each has to offer to the disturbed mind

The psychiatrist today is equipped as doctors fifty years ago were not, with techniques for uncovering the origin and nature of mental stress with theories to mitigate its unbearable quality and with drugs to blunt its physical effects He is less well equipped with means, physical or psychological, for raising the threshold of what can be borne with impunity

The threshold of the bearable varies with the individual Psychologists who subject rats to stresses which would certainly reduce me to tears or frenzy find that they vary strikingly in their stability of character and that by breeding from the most stable and the least stable specimens it is possible to produce two strains which in this particular are wholly distinct all the stable strain supporting their stresses better than any of the other It seems probable that for men as for rats variations in stability have a genetical basis

On the other hand, it is a fact of common observation that humans who have proved unable to cope with a situation have later become equal to it through a change in their mental attitude, though the external situation remains unchanged Sometimes this is due simply to understanding the nature of the conflict A situation cannot be faced until it is realised, psychiatry has not only revealed how much conflict is latent but has developed most welcome means of bringing it to light

Yet a conflict is not necessarily resolved merely by being disclosed It may not be capable of being resolved, it may simply have to be borne Tensions are not only inescapable, but necessary and fruitful It would certainly not be fair to say that psychiatry offers escape from them, while religion offers the strength to bear them, for each in some measure offers both, but the emphasis in psychiatry and throughout the field of mental health is on reducing rather than on supporting stress Possibly this is a limitation inherent in mental science itself It may be that the insight which makes stress worth bearing is different in kind from the insight which merely reveals its nature Or it may be that mental, like general medicine, is hampered because we expect it to make our circumstances easy enough for us, rather than to make us equal to our circumstances

In the preventive field there has been a most notable advance The growing knowledge of our nature has greatly reduced the hazards which we unwittingly create for each other During the last fifty years, the layman's idea of human nature has changed out of all recognition and this has affected every human relationship Parents bring up their children differently, education and penology have been transformed, business management talks a new language Authority, public and private, has adopted a new conception of how human beings work.

Why, then does mental stress still darken life so widely? Shall we blame international tension and the fear of war? I do not believe that this is the answer It is hard to suppose that the shadows of world events lay so darkly across individual minds in the stable-seeming days before the first world war, yet the crises of those days seemed real enough to a generation whose yardstick was the 19th, not the 20th, century In any case the events which divide our wills and wring our hearts and make civil war in our heads are seldom public events We live each in a small world, especially when we are young It is particular human relationships, not the great tides of history, which set our inner stresses

May it not be rather that we are neglecting the more important need? By all means let us reduce the occasions for stress, but stress will remain a characteristic of human life and it may be that if we could remove it, we should lose what most we need Security is not to be found by eliminating challenge, but only in an inner assurance which no challenge can disturb

The easy way to relieve stress is to yoke mental science and modern techniques of persuasion to the task of making everyone well adjusted to everyone else This is not only tempting, it is in a measure useful and indeed necessary For our growing organisation demands ever more conformity, ever more mutually adjusted specialism, ever more acceptance to make it work at all There seems ever less time for doubt and for dissent Yet both Christian and scientific insights warn us that along that road lies mortal danger not only for the individual but for society also

For saints, artists, creative thinkers, and above all martyrs are seldom well-adjusted people, and no civilisation can do without them, least of all ours which changes faster than any has before These are they who incubate tomorrow's orthodoxies through their heretic phase—for all orthodoxies were heresies when they were born These are the deviants, from among whom spir[illegible]tion will find the material for her next big adaptation In every age so far enough have escaped martyrdom to fertilise the next It would be ironic, n we alone were efficient enough to make ourselves spiritually barren

And not for the sake of the saints and martyrs only do we reject the cosy heaven of mutual adjustment Life is an individual affair for each one of us We canno fight each other's battles, feel each other's pain, or se each other's visions The social condition which integral to us does not make us less than our individu selves For each of us, as well as for society and posterity the need to struggle is the chance to grow The world like a dark forge, lighted by the sparks which men stri as they beat the stuff of life into significance on th anvil of circumstance The light is a function of th effort We may make it as bright as day if we hamme hard enough, but we shall never dispense with th need to hammer or live by the light of sparks stru yesterday

It is not enough, then, that we should use ment science to reduce the challenges of stress or even to rev their nature We need its help in reaching the state mind which can bear them and grow by them Th may be those who think this beyond its compass, I not It may never produce guidance, which insight h not already anticipated, but it may, at least, make easier for us to be influenced by what we alre divine

It might, for example, be the greatest help to h some better understanding of how the mind builds its experience We see around us people so limited their mental filing systems that they miss or are hurt most of their experience, while others grow and pr by everything that happens to them We need not surprised, the human organism would be strange ind if any form of organisation were as useful as any oth We would expect, for example, even if every men hospital were not full of evidence to prove it, th complete self centredness would be a most inconveni organising principle for creatures such as we are

Seen from this angle by far the most signific discovery of mental science is the power of love protect and to restore the mind Every film goer, eve newspaper reader, today believes that there is likely be a causal relationship between the deprived child the adult and adolescent criminal He will accept, the authority of science, that love can build for one c a haven of security in a mad world and thus equip it give back the same powerful influence in after life, wh its absence may leave another imprisoned in self capable of no contact with its kind but aggression is not often that the findings of science confirms intuitions of religion in language which does not ev need to be translated This alone, in my view, entit mental science to be regarded not as a rival but as partner in the eternal effort to realise spiritual val in the daily life of men and women—even perhaps in th policies of governments

I declare myself, then, to feel rather more than th modest optimism of Descartes in regard to ment science I am sure that it will help us to keep sane the kind of world which physical science is building f us It might enlighten the choices which invisibly inexorably determine where that world is going Ar in both these functions it seems less likely tha physical science to land us in an inescapable ecologic trap

Yet its most important promise, I believe, is th promise of helping us to conceive of mental health as positive and dynamic condition of mind, to see the pat towards it, to develop the will to achieve it Ment health is not the same thing as spiritual vitality spiritual vision, but I do not believe that they m always belong to different universes of discourse

# FECTS OF ATHEROSCLEROSIS ON THE CORONARY CIRCULATION

J B Duguid
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HEN we attempt to compare the incidence of onary disease in different age groups or in different ions of the community on the basis of post-mortem dings we have to adopt some system of grading l here we encounter difficulties

Atherosclerosis has many variable features and almost y one of them may be taken as a gauge of severity may take for example, the number and extent of lesions, the amount of fatty change or calcification ulceration or the degree of intimal thickening or rowing of the lumina and whereas any one of them y indicate the severity of the atherosclerosis they not all give a true measure of the impairment the coronary circulation, which is what we want to ow in coronary disease in its clinical aspect

The difficulty is that atherosclerosis does not necessarily d to coronary impairment The severest degrees of it e often seen in people with no history whatsoever cardiac disability whereas fatal occlusion may develop cases where the arteries are on the whole relatively e from atherosclerosis We have recently seen this a man aged 31 in whom the only coronary lesion parent to the naked eye was an occluding thrombus on olitary nodule of atheroma in the anterior descending anch.

The dangerous feature in atherosclerosis is narrowing the arteries and if we are to avoid confusion in erpreting our records we must have a clear idea of ere narrowing stands in relation to the atherosclerotic ocess

### Pathogenesis of Arterial Narrowing

Until recently it was assumed that the narrowing of teries in atherosclerosis was due to an overgrowth of the imal connective tissues induced by the presence of s or other noxious agents in the vessel walls, and cordingly the process of narrowing was considered to progressive and likely to increase so long as the disease isted. From this it seemed to follow that the greatest rrowing would be found in the most advanced lesions ich, as we now know, is far from true

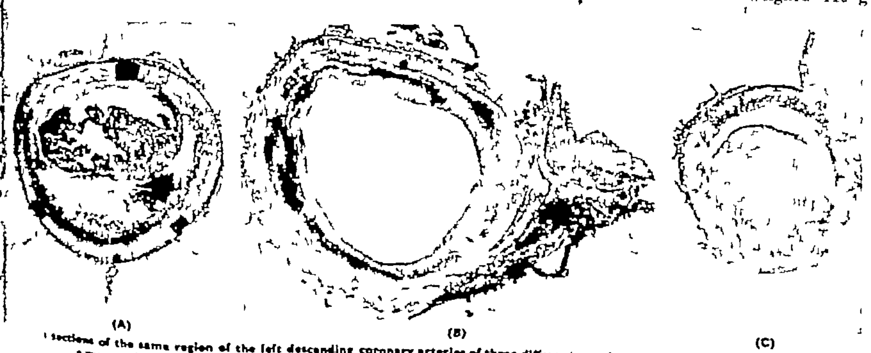
Arterial thickenings, identical with atherosclerosis, are produced by thrombosis (Duguid 1946 1948) When a thrombus forms in an artery it becomes covered with endothelium and thus incorporated in the vessel wall, with the result that when it is organised it forms a fibrous thickening of the intima Since most mural thrombi show some fatty degeneration they give rise to that combination of fatty change and fibrosis which is characteristic of atherosclerosis This does not mean that all atherosclerosis is thrombotic in origin The lesions are an end result common to several different processes (Duguid 1954), but a review of the histology gives every indication that those lesions which involve narrowing are thrombotic, and we must now look on thrombosis not merely as an occasional complication of but also as a factor in atherosclerosis With this in mind narrowing is more easily understood

When a thrombus forms in an artery it occupies the lumen and must therefore reduce the blood stream to some extent but it should be realised that the reduction is not necessarily permanent, because thrombi tend to shrink Under the influence of the blood pressure quite large masses of fibrin will in time become flattened out and condensed with the result that when finally organised they form comparatively inconspicuous thickenings of the intima Thus narrowing may be but transient, and maximal in the early stages of the atherosclerotic process

On the other hand thrombotic thickenings tend to be cumulative and progressive because arterial thrombosis is a recurring condition In the arteries of old people we often see evidence of repeated mural thrombosis, with one fibrin deposit superimposed on another, each adding to the thickness of the vessel wall Consequently we might expect to find the greatest fibrous thickenings in those who have lived longest, and so in general we do but it does not follow that the greatest impairment is to be found in such cases because thickening does not necessarily involve narrowing

### Dilatation of Arteries

In the accompanying figure sections from corresponding points in the left coronary arteries from three different people are shown at the same magnification A is from a man aged 54, who dropped dead in his second attack of coronary thrombosis the first having occurred six months previously B is from a man aged 67 who had no history of cardiac disability but died from hæmorrhage following an operation for cancer and C is from the man aged 31 already mentioned who dropped dead while at work having had no known previous attack, although he was said to have complained of indigestion in his last three weeks The hearts weighed 440 g,



sections of the same region of the left descending coronary arteries of three different people : (A) from a man aged 54 ; (B) from a man aged 67 ; (C) from a man aged 31 Blackened areas in A indicate width of medial coat at three points. (× 11)

410 g, and 350 g respectively, but, although the left coronary arteries were equally preponderant in all three, that from the oldest of the three men is by far the largest When we compare the changes in these vessels we can see something of the effects of intimal thickening

In section A a crumbling mass of fibrin in the lumen, representing the fatal occlusion, and a crescentic fibrous thickening of the intima below can be seen The thickening does not entirely encircle the lumen but leaves a segment of the wall at the upper part unaffected, and there the medial coat is thicker than elsewhere In considering the significance of this, certain principles of arterial histology have to be taken into account MacWilliam and Mackie (1908) have shown that arteries contract after death, and the amount of contraction is indicated by the thickness of their medial coats compared with the size of their lumina, the media being thicker when the vessels are contracted This post mortem contraction is not simply a collapse of the arteries on removal of the blood, nor is it a rigor mortis, but it is a true tonic contraction of the muscle, the vessels being capable of reacting to stimulation, sometimes for as long as two days after death Section A shows that the relatively thin media where the intima is thickened denotes a reduced contraction in that particular segment of the vessel wall

Thinning of the media in relation to intimal thickenings has long been recognised as a feature of atherosclerosis, and has been interpreted in various ways, but in considering it we should take into account another important principle Arteries are elastic tubes, able to maintain their appropriate calibre in face of a constantly pulsating internal pressure by reason of their ability to dilate and recoil again to their original size with each pulse wave The recoil is not a muscular contraction but a purely elastic movement, depending on the inherent resilience of the vessel walls, and anything that impairs this quality will interfere with the movement and cause the vessels to remain more or less dilated Post mortem contraction and elastic recoil are different functions, the former being a tonic contraction of muscle and the latter merely a physical reaction, but both are measures of the range of mobility of the vessels, and the reduced contraction at the thickened part of section A indicates a loss of resilience, which has kept that particular segment dilated Section B shows this effect carried further, because the intima round the whole circumference is thickened, the vessel is widely dilated, and, in spite of the intimal thickening, its lumen is greatly increased

There seems to be little doubt that these appearances reflect in a large measure the state of affairs in life, and we may take them as evidence that atherosclerosis ultimately leads to dilatation of the arteries hence any narrowing that results from thrombosis in the early stages tends to be cancelled out It is therefore not surprising that the arteries of aged people, as Aschoff (1938) remarked, are usually dilated

### Danger of Atherosclerosis

It is in the early formative stages that atherosclerosis is dangerous, and a man aged 40 with a recent thrombus in his coronary system may be in far greater danger of sudden death than a man aged 70 with widespread lesions in the arteries Consequently the records of atherosclerosis in general-hospital deaths are not likely to give a true indication of the incidence of coronary impairment in the community Atherosclerosis is almost universal in adult life, and, if we are to judge from histology, much of it is thrombotic in origin, but even thrombosis does not necessarily involve impairment of the circulation The great majority of arterial thrombi are too small to interfere with the blood flow, and their only effects are to produce fibrous thickenings which by reducing elasticity, lead to relatively harmless dilatation It is when large thrombi form in clo succession that there is danger, and so, from whatever aspect we view it, the essence of coronary disease thrombosis

Why thrombi form in the first place, and what relationship they bear to a primary fatty or other change in th vessel walls, are questions we must pass over for th present Mural thrombosis seems to be common to mos people who live beyond middle age, and is in mo instances harmless, hence the more immediate an crucial questions are how is the process usually kep within safe limits, and what are the conditions whi sometimes allow it to exceed these limits and produ occlusions ?

The answers to these questions are more likely to found in the clinical study of thrombosis than in th morbid anatomy of atherosclerosis, which, after all, in most cases but a late sequel of thrombosis, and we are to use the general records to best advanta we ought to direct our attention more to narrow than to the other features of atherosclerosis Unfortun ately this makes the inquiry more difficult beca arterial thrombosis is in most instances localised, a the narrowing which results from it is usually confi to short lengths of the vessels, often no more tha millimetre or two in extent Therefore to detect s narrowing the most exhaustive search through all major branches of the coronary system is requi irrespective of whether the vessels appear grossly ath sclerotic or not Unless we can be sure that this has be the practice in hospitals in the past, their records atherosclerosis must be regarded as of doubtful va in the assessment of coronary impairment

### Re-establishment of Circulation

Another point to be learned from the histology coronary disease is that total occlusion is not necessa irreversible It has been assumed that survival of myocardium in cases of occlusion depends on the establi ment of a collateral circulation, but a glance at section will show that there is another mechanism to be ta into account This section is from a point immediat below the fatal occlusion, and the terminal thromb is not included, but the lumen is occupied by a mass fibrous tissue which is obviously an old organ thrombus Judging by its shape we must suppose th it originally filled the lumen, but it is now part separated from the wall, allowing a channel for blood to pass Since there was no old infarct in appropriate area of the myocardium in this case, may conclude that this partial restoration of the circ tion must have been effected sufficiently early to a infarction, and that, if there had been no further thro bosis, the man might have continued his normal activi indefinitely In due course, under the influence of blood pressure, the channel would no doubt ha gradually widened and the fibrous mass shrunk, wi the result that finally the circulation might have be largely restored

Histological appearances of this kind are common coronary thrombosis, and we may take them as represen ing an emergency mechanism by which total arrest the circulation is not infrequently relieved Two possi factors may be involved in the mechanism, retracti of the thrombus, and relaxation of the vessel but it obvious that the relaxation is the essential Anyon who has studied the behaviour of living arteries und the microscope must have been impressed with th remarkable changes in diameter brought about by alter tions in tone, and will appreciate how a sustained spas of the vessel could prevent the opening of a channel thus kind In view of these appearances should not ou first concern in cases of coronary thrombosis be t encourage relaxation of the vessels ? It is perhaps a pit t the recognition of thrombosis as a cause of cardiac n has led to the rejection of the use of the nitrites uch cases.

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# HE TREATMENT OF CHRONIC AMŒBIC DYSENTERY WITH ANTIBIOTICS IN COMBINATION WITH OTHER DRUGS

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ALTHOUGH several drugs are available for the treat- nt of amœbiasis, there is still no single one that will adicate it from the bowel in all cases

Usually gr 4 of emetine will quickly control an acute tack of amœbic dysentery, but the amœbic cysts are t affected hence prolonged courses of emetine do not adicate amœbic dysentery The chief use of emetine in the treatment of amœbic hepatitis

Chloroquine is also useful in the treatment of hepatitis, ut it is so rapidly absorbed in the upper bowel that it es not affect intestinal amœbiasis.

The other drugs used in amœbiasis can cure 70–85% the acute and less chronic cases of amœbic dysentery t not the chronic cases

Chronic amœbic dysentery responds only to a combina n of drugs, and even then repeated treatments may necessary Some of the most successful combinations re evolved during the 1939–45 war by American and itish workers.

The U.S Army plan of treatment consisted in a pre minary course of penicillin and succinyl sulphathiazole eliminate secondary bacterial infection from the eased bowel wall, followed by emetine daily for 4–6 ys, and subsequently emetine bismuth iodide for days without a break. During the course of emetine muth iodide the patients also received a daily retention ema of chiniofon sodium During the succeeding days either di iodohydroxyquinoline or carbarsone s given The patient was kept in bed throughout the eatment If cure was not obtained with a single course cond was given after an interval of 10–12 days.

Later, the British workers omitted the chiniofon dium enemata and after a preliminary course of nicillin and sulphaguanidine administered emetine r 2 days followed successively by emetine bismuth dide for 10 days and carbarsone for 8 days. In addition e patient received di iodohydroxyquinoline throughout e course of treatment The results of this treatment re very good. In 103 cases of chronic amœbic dysentery ated by me in seven years the immediate cures were 1 % and after 3–6 months follow up 60·0%

A patient who did not respond to two courses was not ely to respond to a third a change in combination drugs was necessary Further the treatment did not ways eradicate the amœbiasis completely because of the 103 patients subsequently developed amœbic patitis from 6 months to 5 years after treatment

Since then aureomycin and oxytetracycline have been nd to combat the secondary infection and to destroy th the trophozoites and the cysts; so it has become ssible to substitute them for penicillin succinyl lphathiazole emetine and emetine bismuth iodide nd thus to make the treatment more effective and less ensive to the patient

With this background an initial combination of aureo ycin carbarsone di iodohydroxyquinoline and chloroquine, and, in some cases, a subsequent combination of oxytetracycline, carbarsone, and mepacrine were tried

## Material

32 patients with chronic amœbic dysentery of 3–12 years' duration were treated 27 being males and 5 females The diagnosis was based on previous history and findings and results of clinical, stool, and sigmoidoscopic examinations. Only cases found positive by stool and/or sigmoidoscopic examinations were selected for trial

13 patients had previously had two or three courses of the U S or British Army plan of treatment described above and 19 had had no standard treatment but had taken singly or in combination, carbarsone, iodochloro hydroxyquinoline ( Vioform ') di iodohydroxyquinoline, emetine bismuth iodide, emetine, aureomycin, and oxytetracycline rather haphazardly and inadequately several times

7 had associated hepatitis or hepatic abscess, with the liver palpable 2–5 finger breadths below the costal margin in the mid-clavicular line on inspiration 3 of those 7 patients with hepatitis and 10 others had easily palpable and tender cæcum and/or descending colon 1 had clinical jaundice All had diarrhœa, abdominal tenderness, flatulence, indigestion, anæmia, and avitaminosis

## Method

*Treatment*

Anæmia and avitaminosis were treated with loading doses of intravenous iron and vitamins There were no special restrictions on diet. A high-caloric high protein diet rich in vitamins and leaving little residue was given according to the requirements and tolerance of the patient The patients rested, preferably in bed, throughout the course of treatment

The antidysenteric treatment consisted of aureomycin 500 mg, carbarsone 0 25 g di iodohydroxyquinoline 0 6 g and chloroquine 0 2 g all given together at 6 A M, 2 P M and 10 P M for 6 days followed without a break by di iodohydroxyquinoline and chloroquine only for 14 days The 6 A.M and 10 P M doses were given with a drink of milk, and the 2 P M dose followed luncheon

If any residual symptoms and signs were left behind after 6 weeks from the start of treatment irrespective of a negative stool a second course consisting of oxytetra cycline 500 mg carbarsone 0 25 g and mepacrine 100 mg all administered together at 6 A M 2 P.M, and 10 P M for 6 days, was given This was, however done in only 5 cases in which there was slight residual tenderness over the cæcum or over the descending colon and stools were still positive for occult blood but negative for trophozoites and cysts

*Follow-up*

All the patients were followed up for at least 3 months During the first month the patients were examined once a week, and during the second and third months once a fortnight for clinical improvement

Stools were examined on 3 consecutive days at the end of the first and second months and on 7 consecutive days at the end of the third month of treatment They were examined fresh for trophozoites and by con centration method for cysts. The last examination for cysts was preferably done after a saline purge

Sigmoidoscopy was done on all the patients except 3 females at the end of 3 months follow up along with tests for occult blood in the stools for evidence of residual ulceration Appropriate blood-counts were also made in cases with anæmia and hepatitis

Subsequent contact with patients was irregular but 20 of them have been followed up from 8 months to 2 years

## Results

*Clinical improvement.*—There was progressive clinical improvement in 23 cases Diarrhœa abdominal tender ness, indigestion, and enlargement and tenderness of the liver, if present, mostly subsided before the end of the course of treatment or shortly after In 4 cases diarrhœa continued for 6–14 days after completion of treatment, but the stools were negative in all of them Progressive diminution in the number of stools in 3 of them suggested that diarrhœa was a secondary effect of drugs, probably aureomycin, and it was easily controlled with small doses of tincture of chloroform and morphine In 1 case diarrhœa continued for 3 months Barium radiography suggested in this case a residual chronic appendicitis, and the effect of its removal was dramatic In another 5 cases tenderness and thickening over the cæcum and descending colon had not completely disappeared at the end of 6 weeks and progress appeared to have stopped, although the stools were negative These patients were given a course of oxytetracycline, carbarsone, and mepacrine as described above, and in another 3–6 weeks they were symptomless All the patients put on 4–8 lb in weight a month and rapidly improved in health

*Stool examinations*—All the cases were negative at the end of the first month's check and thereafter during the follow up

*Occult blood*—Tests for occult blood were negative in all the cases at the end of 3 months' follow-up

*Sigmoidoscopy*—All visible ulcers had healed within 3 months

### Discussion

The drugs used in the treatment of amœbiasis are of surprisingly divergent constitution and can be classified into five groups (1) emetine and emetine bismuth iodide, (2) pentavalent arsenicals (e g, carbarsone, dithio derivatives of carbarsone, and bismuth glycolyl arsanilate ('Milibis'), (3) hydrogenated hydroxyquinolines (e g, chiniofon sodium, iodochlorohydroxyquinoline, and di iodohydroxyquinoline), (4) aminoquinolines (e g, chloroquine); and (5) antibiotics, of which aureomycin, oxytetracycline, and fumagillin are promising

The uses of emetine and of chloroquine have already been described

The dithio derivatives of carbarsone are more effective and less toxic than carbarsone Milibis is almost unabsorbable, hence a high concentration of it can be obtained in the lumen of the large intestine with about a tenth of the toxicity of carbarsone It is therefore bound to supersede carbarsone

Iodochlorohydroxyquinoline is superior to chiniofon as an amœbicide, but di iodohydroxyquinoline is still better and hence generally used

Frye et al (1952) found oxytetracycline to be superior to aureomycin in the treatment of amœbiasis, the cure-rates were 97 5% and 70 7% respectively Armstrong et al (1950), however, reported 94%, and Calero (1951) 86%, successes with aureomycin In chronic amœbic dysentery in veterans of the 1939–45 war Hall (1951) obtained a cure-rate of 70% Comparative studies with fumagillin in acute ulcerative amœbiasis in Africans by Elsdon-Dew et al (1953) indicate that aureomycin is superior to fumagillin

Emetine bismuth iodide, the pentavalent arsenicals, hydrogenated hydroxyquinolines, and the antibiotics act on both trophozoites and cysts

The combination of drugs used in the present trial theoretically promised good results and achieved them in practice The substitution of its dithio derivatives for carbarsone may produce even better results

### Summary

32 cases of chronic amœbic dysentery, all failures with previous therapies, were treated with a combination of aureomycin, carbarsone, di-iodohydroxyquinoline, and chloroquine for 6 days, followed without a break by di iodohydroxyquinoline and chloroquine for 14 days

In 23 cases the symptoms subsided before the end of the course of treatment or shortly after

4 cases had residual diarrhœa In 3 it was presumably due to the effect of aureomycin and subsided spontaneously *in 6–14 days after completion of treatment* In the 4th case appendicectomy relieved it

In the remaining 5 cases the cæcum and descending colon were still tender, an additional course of oxytetracycline, carbarsone, and mepacrine proved successful.

Thus, finally, all the cases were found to be cur at the end of 3 months' follow-up by clinical, stoo sigmoidoscopic, and occult-blood tests

Subsequent follow-up of 20 cases from 8 months t 2 years showed that the cure was permanent

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# CONGENITALLY SHORT FRENULA OF UPPER LIP AND TONGUE

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Short frenula of the upper lip and tongue are com congenital deformities, but as they cause only m disfigurement and disability they are often ignored.

### Short Frenulum of Tongue

Not many years ago, if a child was late in acqui speech, the mother was told by the neighbours that must be "tongue tied" The frenulum of the ton was then "snipped" with scissors

In order to discourage this barbarous practice so have said that tongue tie requires no operation beca it does not exist Actually, however, a congenital short frenulum linguæ (fig 1) is relatively common and, though it does not prevent a child from acqui speech at the normal age, it does sometimes ca minor difficulties—e g, in the pronunciation of cer consonants

Division of a tight frenulum, without anæsthesia, b snip with the scissors soon after birth is either danger or ineffective If the snip is adequate it is dangero because the profunda linguæ vein is usually divide If the snip is inadequate, it is ineffective because

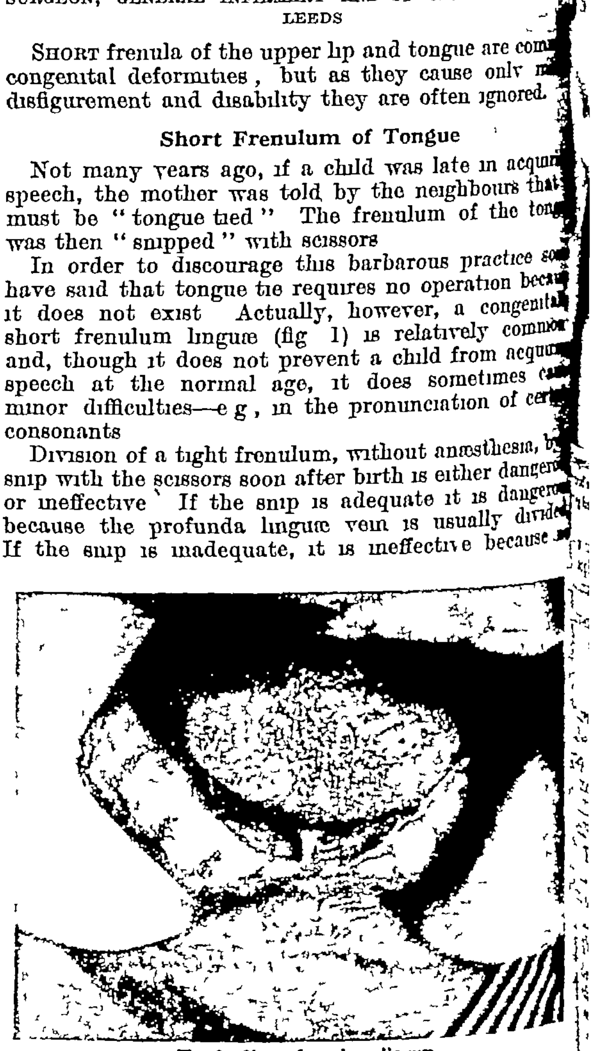

Fig 1—Short frenulum linguæ.

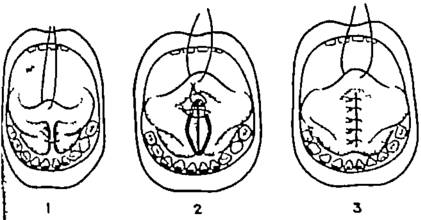

Fig 2—Steps in operation for repairing short frenulum linguæ.

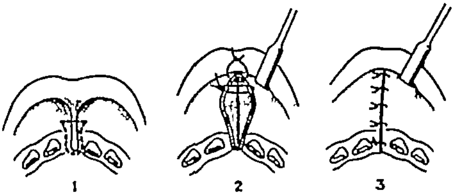

Fig 4—Steps of operation for repair of short frenulum of upper lip.

lasting benefit is achieved On the other hand I think that before he goes to school the child s disability should if possible be removed and this can be done by the following operation

Under intratracheal anæsthesia with a throat pack in position, the tight frenulum is divided transversely (fig 2) The mucosa on each side of the incision is mobilised by under cutting with blunt nosed scissors any deep bands of tight fibrous tissue should be divided until the tip of the tongue is free to protrude to the normal extent Bleeding vessels are carefully ligatured. By traction with a hook in the extremity of the wound nearest the tip of the tongue a longitudinal suture line can be made Lateral mattress stitches of chromic catgut inserted with a fine cleft palate needle are used to close the wound and to repair the defect A little penicillin cream is applied to the suture line and the child goes home next morning No special after treatment is required

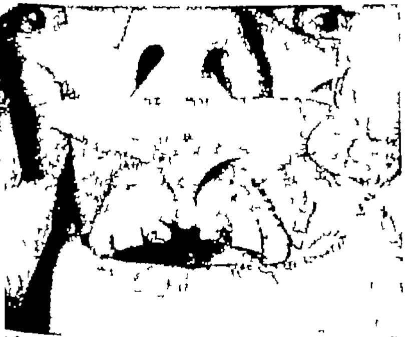

Fig 3—Congenitally short frenulum of upper lip showing fibrous bar protruding as far as free margin of gum in midline thus preventing fusion of alveolar processes of maxillæ.

Twenty-six babies have been treated in this way and the results appear to have been satisfactory

## Short Frenulum of Upper Lip

A congenitally short frenulum of the upper lip (fig 3) is invisible. It causes no disability but gives rise to a wide gap in later life between the permanent upper central incisor teeth A wide gap here is conspicuous when smiling and the patient realising this may refrain from smiling unless provocation is extreme—which seems a pity The wide gap is caused because the short fibrous frenulum of the upper lip extends as far as the free margin of the gum between the two alveolar processes of the maxillæ this prevents bony fusion in the midline A simple little operation in childhood will remedy this

Under general anæsthesia with a throat pack in position the soft tissue is excised from the gap between the two alveolar processes of the maxillæ (fig 4) The bone is roughened with a small periosteal elevator A transverse incision is made across the tight frenulum beneath the lip The mucosa is mobilised on each side and the wound is repaired by a longitudinal suture line in the same way that the tight *frenulum linguæ is treated*

During the last two years I have used this method on sixteen occasions and the parents have been pleased

The cause of this congenital defect is unknown but it may be related to median cleft of nose and median harelip because median harelip is always associated with a short frenulum of the upper lip Moreover in patients with lateral harelip a tight frenulum of the upper lip is often present (*fig 5*)

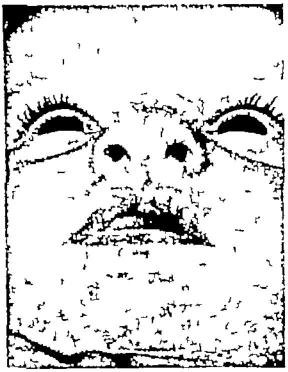

Fig 5—Median harelip with short frenulum of upper lip.

### Prolapsing Mucosa of Upper Lip

An uncommon congenital abnormality to be distinguished from short frenulum is a condition in which the lining mucosa dips below the vermilion border (fig 6) So far as I am aware, this has not yet received an official name and though the term congenital prolapsing mucosa of the upper lip is cumbersome it seems to describe it best

In the three patients whom I have treated the deformity was repaired by making a horizontal incision in the lining mucosa from one end of the lip to the other I excised

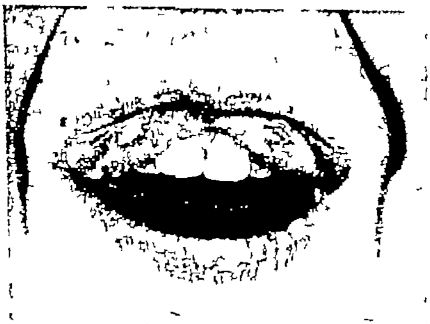

Fig 6—Congenital prolapsing mucosa of upper lip.

an ellipse of the prolapsing mucosa I then sutured the wound with a horizontal suture line, using "end-on" mattress stitches of chromic catgut The first deep bite included the orbicularis oris muscle, and the more superficial bite only the mucosa

### Conclusion

The indications for operation on a short frenulum linguæ are a little indefinite, and many surgeons with adequate reasons might advise against operation I believe, however, that a simple operation will remedy the defect with negligible risk and pleasing results

The indications for operation on a short frenulum of the upper lip are definite the fibrous tissue preventing bony fusion of the alveolar processes of the maxillæ should be excised This will prevent disfigurement in later life by wide spacing of the upper central incisors

## MEDIAN-NERVE PALSY ASSOCIATED WITH ACUTE INFECTIONS OF THE HAND

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Two cases have recently been seen at University College Hospital in which median nerve palsy resulted from acute pyogenic infection of the hand We can find no reported account of such an association, although it is well known that interference with the function of the median nerve may result from tuberculous infection of the flexor-tendon sheaths in the carpal tunnel

### Case-reports

#### CASE 1

A housewife, aged 58, was admitted to University College Hospital on April 4, 1954, having cut her right thumb two days previously on a broken milk bottle About sixteen hours after this injury she developed severe pain in the palm of the hand and in the wrist Her doctor gave her an injection of penicillin, but as the pain gradually became worse he referred her to hospital She did not complain of pain in the thumb at any time She gave a past history of gout affecting the left foot, and she also stated that she had had "rheumatism" of both hands for many years

*Examination*

Temp 100 6°F, pulse rate 80 per min In her right hand there was a small clean puncture wound in the centre of the interphalangeal flexor crease of the thumb The thumb and all fingers were swollen, there was œdema of the dorsum of the hand, and the whole hand felt hot There was slight redness and tenderness over the thenar eminence and at the front of the wrist The fingers were flexed into the palm and active extension was impossible, attempted passive extension caused severe pain in the distal part of the palm and also just above the wrist Movements of the thumb were full and painless There was slight limitation of extension at the wrist She complained that her fingers felt numb, but no sensory loss was found anywhere in the hand There was no lymphangitis or lymphadenitis The left hand showed the changes of early osteo arthritis with Heberden's nodes and slight limitation of extension of the fingers

*Treatment*

Immobilisation and elevation of the hand and intramuscular penicillin (500,000 units six hourly) failed to control the pyrexia and local condition, and after three days aureomycin (250 mg six-hourly) was substituted for penicillin Six days after admission the fingers were more tightly flexed into the palm and there were signs of localisation of the infection at the [illegible] thenar eminence After ten days the pain in the wrist and palm was subsiding, the temperature was normal, and the local signs in the thenar eminence had cleared up There was still no evidence of any sensory loss. Daily physiotherapy was started and antibiotics were discontinued. On April 23 (nineteen days after admission), however, pain returned to the wrist and palm, and the temperature rose to 100°F again At this time induration was palpable in the distal part of the palm opposite the ring and little fingers, and for the first time there was sensory loss—blunting to pinprick, and loss of light touch in the thumb and radial two and a half fingers Physiotherapy was continued, and over the next few days the sensation appeared to improve, but then it deteriorated again, until on May 3 (four weeks after admission) anæsthesia in the median nerve distribution was almost complete and there was in addition paresis of the flexor and abductor pollicis brevis At this stage there was increased swelling just above the wrist and induration of the skin at the level of the distal palmar crease on the ulnar side of the hand It was decided that the median nerve should be explored.

*Operation*

Operation was undertaken (D B) on May 5 (one month after admission) under general anæsthesia, with a bloodless field Through an incision along the medial two thirds of the distal flexor crease of the wrist and then carried at right angles to skirt the base of the thenar eminence, the transverse carpal ligament was exposed and completely divided The flexor tendons were surrounded by gelatinous looking granulation tissue which appeared to have replaced the tendon sheaths The median nerve was flattened and almost bl from a point about halfway along the carpal tunnel to the lower edge of the retinaculum, beyond which it became normal Distally the granulation tissue extended deep to the palmar fascia, and pressure over the indurated area in the palm produced a flow of thin pus, which was cultured The median nerve was dissected free, and the granulation tissue was excised leaving the tendons bare, this excision was carried as far as the distal palmar crease The tendons themselves for the most part appeared normal, but in places were roughened and hæmorrhagic The skin was loosely sutured without drainage The hand was again splinted and elevated and a further course of penicillin was started

*Progress*

The patient's convalescence was satisfactory On the following day she said that her fingers felt less numb, but on examination no change was found Sutures were removed on the eighth postoperative day, the wound healing by first intention Culture of the pus yielded *Staphylococcus albus* sensitive to penicillin and aureomycin Microscopy of tissue removed at operation showed the changes of non specific subacute inflammation with young fibrous tissue and endarteritis obliterans of the arteries Physiotherapy was resumed after removal of the sutures, and the range of movement the fingers improved steadily When discharged from hospital on May 19, the patient was complaining of paræsthesiæ in the thumb and radial two and a half fingers, the sensation of light touch was completely absent, but there was some appreciation of pinprick, except in the thumb She has continued to attend hospital for physiotherapy, and has been examined regularly When last seen, on Nov 12 (six months after the operation), the scar was well healed, inconspicuous and supple, and there was no bulging at the site of division of the retinaculum Movements of the wrist and digits were painless and full except for slight limitation of extension of the fingers There was some impairment of light touch sensation and an abnormal tingling response to pinprick over the tips of the fingers and thumb, proximally, sensation was normal It had been noted previously that return of sensation was patchy and did not appear to proceed proximo-distally in a regular manner There was slight wasting of the thenar eminence the short flexor and abductor of the thumb showed normal power, but opposition was weak The patient herself was pleased with the result and announced that she had been able, the previous week, to decorate a room unaided.

#### CASE 2

A housewife, aged 53, was admitted to hospital on May 2 Thirty six hours previously she had been pruning some rose trees and thought that she pricked her right thumb on a thorn. Two hours after finishing her gardening she noticed pain and swelling of the right thumb Shortly afterwards the pain left her thumb and was felt in the palm of the hand opposite the ses of the index and middle fingers, and at the same time he noticed numbness in the tips of the thumb and index and iddle fingers. She went to bed and passed an uncomfortable ight. On the following morning the thumb was swollen and ightly red, and the pain in the palm of the hand had increased he was seen by her doctor who gave her an injection of enicillin (1 000 000 units) and arranged her admission to niversity College Hospital

*Examination*

Temp 99°F; pulse rate 90 per min. The right hand was eld in the position of rest. The right thumb was considerably wollen and slightly red but was not tender but there was enderness to deep pressure over the thenar eminence. There as no swelling of the other fingers. On the front of the wrist ere was an area of inflammation about one inch in diameter st proximal to the distal flexor crease on the ulnar side ovements of the thumb were full and painless all the her fingers could be fully extended actively but this caused vere pain in the forearm just above the wrist. The patient mplained of numbness in the thumb and lateral two and half fingers extending proximally as far as the metacarpo halangeal joints, and on examination there was blunting to inprick and loss of light touch. There was no lymphangitis, t an epitrochlear gland was palpable. Because of the edian-nerve involvement it was decided to explore the rist.

*irst Operation*

At operation (J. F. B. C.) under general anæsthesia on May 2 transverse incision one inch long was made across the distal lexor crease of the wrist, and when deepened this released ear yellow fluid. Pressure over the thenar eminence produced urther fluid, and a specimen was taken for culture (subse uently found to be sterile). The transverse carpal ligament as divided distally for half an inch and the tendons and ian nerve appeared normal at this level. It was thought adequate decompression had been effected and nothing her was done. The wound was left open and a plaster t slab was applied over dressings. A course of intra cular penicillin (250 000 units six hourly) and strepto m (0·5 g twice daily) was started and the hand and arm were elevated.

*gress*

hree days later the cellulitis at the wrist and tenderness r the thenar eminence had gone and the wound appeared an; but the index and middle fingers were held in flexion ive extension being impossible and passive extension remely painful. The thumb still had a full range of painless ement and the swelling of this digit had decreased. re now was however complete sensory loss in the area viously described, and it appeared that further decom ession of the carpal tunnel was required

*ond Operation*

On May 6 under general anæsthesia and with a bloodless ld, the previous incision was reopened (J. F. B. C.) and from e centre of this a second incision was made distally along convenient skin crease to follow the base of the thenar inence for one and a half inches. The incision was deepened expose the transverse carpal ligament which was then ided completely to expose the tendons and median nerve here was some yellow serous fluid present. The tendon eaths were a little œdematous, but the tendons appeared rmal. The median nerve at the distal end of the tunnel ppeared to be narrowed, as if by compression there was tchy pink discoloration extending proximally for half an ch. A further specimen of fluid was taken for culture (again terile). The skin wound was closed, a plaster front slab pplied over dressings and the arm again elevated

*Progress*

Penicillin was discontinued following an allergic reaction ut streptomycin was continued for fourteen days. After the second operation the stiffness and pain on movement radually left the fingers, but these remained swollen for two eeks. The wound healed by first intention. Active move ents and wax baths were started on the sixteenth day and ovements of the fingers gradually improved. There was at his time no change in the sensory loss and the patient still omplained of a dull pain across the palm of the hand which was relieved to some extent by warmth. She was discharged from hospital on June 10 when extension of the fingers was almost full and she could make a reasonable fist. The hand throbbed a little when held down and it ached across the palm at night. Sensation had begun to return in the thumb and lateral half of the ring finger and she experienced pins and needles in these fingers. Sensory loss remained complete in the index and middle fingers. There was no obvious loss of motor power. She continued her physiotherapy as an out patient and was examined fortnightly. Movement of the fingers was fully restored by the end of July when swelling of all the digits had completely subsided. The sensation gradually returned to the thumb and fingers, spreading peripherally and recovery was complete at the end of October; the return of sensation was heralded by considerable cramp like pain and pins and needles. When last seen on Nov. 7 the patient said that in cold weather the thumb and index and middle fingers were blue and felt colder than the rest of the hand. The division of the carpal ligament has not interfered with function and the linear scar is barely visible

## Discussion

The similarity between these two cases is striking. The early symptoms and the effect on the median nerve were very much alike and differed only in the time of onset. The findings at operation were rather different but possibly these represent two stages of the same disease process, for case 2 was operated on shortly after the original injury, whereas case 1 was operated on after an interval of four weeks. This difference in the time of operation appears to have had little effect on the rate of recovery of the median nerve

The cause of this condition is obscure but it seems likely that in both cases infection of the sheath of flexor pollicis longus resulted from a penetrating wound of the thumb, although in neither case was there unequivocal evidence of acute tenosynovitis of this sheath. Judging from the rapid onset of flexion of the fingers with extreme pain on attempted extension it would appear that infection spread from the radial bursa to the ulnar bursa surrounding the tendons of the deep and superficial flexors of the fingers. In both cases antibiotics were administered early and probably this was responsible for the sterilisation of the inflammatory fluid in case 2, and for the prevention of an overwhelming infection in both cases. We suggest that interference with the function of the median nerve resulted from compression by inflammatory exudate in the radial and ulnar bursæ deep to the flexor retinaculum, causing ischæmia of the nerve. An alternative explanation is that the signs were produced by spread of infection to the nerve itself with or without thrombosis of the arterial supply of the nerve. We prefer the hypothesis of compression ischæmia, for several reasons. Firstly in both cases the appearance of the nerve at operation suggested compression. Secondly the fact that in both cases the changes in the nerve were strictly confined to the carpal tunnel and did not extend to the proximal and distal limits of the synovial sheaths does not suggest direct spread of infection from these sheaths to the nerve. Thirdly, in case 1 the comparatively late onset of nervous signs at a time when the infective process had passed its zenith suggests a pressure effect rather than an infective neuritis. Lastly the long period required for recovery and the fact that despite the different timing of the operation in the two cases this period was almost exactly the *same* are most easily explained on the basis of an ischæmic lesion of the nerve.

In retrospect it appears that in case 1 operation was delayed too long and in case 2 the first operation failed to decompress the carpal tunnel.

As a result of our experience with these two cases, we suggest that any case of acute infection of the hand complicated by signs of interference with the function of the median nerve should be treated by division of the transverse carpal ligament. This division should be done early before the nerve has been irreversibly damaged and it should be *complete* to provide effective decompression. Complete division can be safely attained only through an extensive skin incision. In neither of these two cases did any disability result from d carpal ligament, and in neither case was there any difficulty in obtaining healing by first intention and an inconspicuous scar

### Summary

Two cases of acute hand infections, following minor trauma to the thumb, were complicated by median-nerve paralysis

This paralysis was probably due to pressure ischæmia of the median nerve in the carpal tunnel

It is suggested that such cases should be treated by early and complete decompression of the carpal tunnel

We should like to thank Mr C W Flemming and Prof R S Pilcher for permission to publish these cases and for encouragement and help in the preparation of this paper

# THE BASAL METABOLIC RATE DURING SLEEP

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ESTIMATION of the basal metabolic rate (B M R) is probably the simplest way of estimating the activity of the thyroid gland But, because of the difficulty of consistently achieving the basal state, particularly with nervous patients, it has never been an entirely satisfactory test, and is at the moment less favoured than other and newer diagnostic procedures

If the technique of Robertson and Reid (1952) is used and duplicate estimations are done daily under ideal surroundings until two readings are obtained that agree within 5%, the results can be reliable In practice this is not usually possible, and some less time consuming procedure has to be found if the B M R is to retain its usefulness Attempts have therefore been made to ensure the patient's basal state by sedation

Bartels (1949) showed that thiopentone anæsthesia reduced the mean B M R of 17 healthy people from + 4% to − 9% but left that of 13 thyrotoxic patients in the hyperthyroid range He thought that the procedure might be useful for distinguishing between nervous and thyrotoxic patients

Rapport et al (1951) suggested a safer method the intravenous injection of pentobarbitone sodium ('Nembutal'), which induced only sleep and so avoided the risks of anæsthesia They showed that the B M R so obtained agreed with the clinical diagnosis in 91% of 200 patients—a much higher correlation than they obtained with the B M R of patients awake We have found that during sleep the metabolic rate is consistently basal

We used pentobarbitone sodium in 73 patients according to the method of Rapport et al (1951), and oral amylobarbitone sodium ('Sodium amytal') in 53 patients, to measure their B M R during sleep, and we report here the encouraging results

### Methods

All the estimations of B M R were made with the Benedict-Roth machine on inpatients who had fasted overnight

*Intravenous Pentobarbitone Sodium* —On the first day a tracing was obtained without sedation This was repeated next morning, and immediately thereafter the patient was put to sleep with pentobarbitone sodium and a third tracing was obtained For this last estimation the patient lay on her left side near the edge of the bed, and pentobarbitone sodium 1 ml (500 mg in 10 ml.) was injected into the left antecubital vein, followed by 0 5 ml every minute until the patient was asleep The dose varied from 125 to 375 mg but was usually about 200 mg The depth of sleep varied somewhat from one patient to another but never approached the condition of surgical anæsthesia The rubber mouth piece was sometimes introduced before the patient went to sleep, at other times it was inserted during sleep Occasionally it proved necessary to hold the lips round the mouthpiece to prevent leakage, but we did not make a practice of plastering up the mouth as suggested by Bartels (1949) When the test had been completed, the patients were often given an intramuscular injection of amphetamine sulphate 20 mg, but they remained drowsy and sometimes confused until the afternoon They did not vomit

*Oral Amylobarbitone Sodium* —The B M.R was estimated without sedation on two consecutive mornings as described above On the third day the patients were given oral amylobarbitone sodium gr 3 every hour from 6 A M until they were unrousable (three or four doses), after which tracings were obtained in the same way as after intravenous pentobarbitone sodium

*Patients Studied* —The B M R was estimated during sleep in most of the patients admitted for investigati of thyroid function since June, 1952 The presen analysis includes all those cases in which sleep was satisfactorily induced, attempts to induce sleep with pentobarbitone sodium in 2 cases, and with amylobarbitone sodium in about 30 cases, failed The patien treated with pentobarbitone sodium were subsequen grouped into six clinical categories (definite and possib myxœdema, euthyroid, definite and possible hyperthyroidism, and "nervous") in the light of clinical findings, the response to treatment, and the results obtained with radio iodine and other tests The patients treated with amylobarbitone sodium were fewer and were only subdivided into hypothyroid, euthyroid, and hyperthyroid

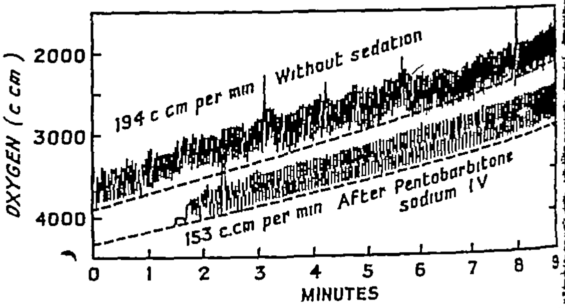

**Fig 1—Two tracings obtained at an interval of about 15 minutes the same patient: the upper one without sedation, and the low one with the patient asleep after intravenous injection of pent barbitone sodium**

### Results

The tracing made during sleep was usually straighter and smoother than when the patient was awake (fig 1), and the excursions tended to be smaller and more regular, though this was not invariably so Fig 2 shows the effect of intravenous pentobarbitone sodium on the metabolic rate in the six categories of patients studied In each column the left hand values represent the lowest B M R obtained without sedation, and the right hand values represent the B M R during sleep Each result is expressed as a percentage of the appropriate Robertson and Reid (1952) standard mean The marked area covers 85–115% of this standard, or the normal range * It will be seen that the B M R during sleep of

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* The normal range is taken by Robertson and Reid (1952) to extend to 2 S D either side of the mean, this is usually about ± 15%

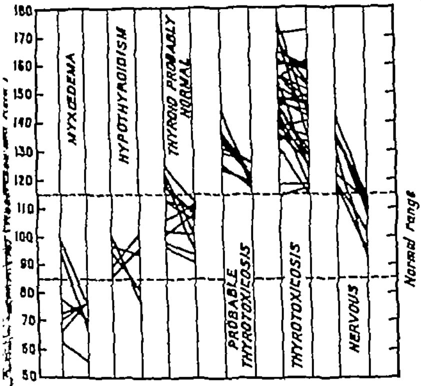

Fig. 2—Effect of intravenous pentobarbitone sodium on the B.M.R. Left-hand point represents lowest estimation of B.M.R. in patient awake, and right-hand point B.M.R. during sleep. Each result is expressed as a percentage of the appropriate Robertson and Reid standards. Interrupted lines mark the approximate limits of the normal range.

thyroid patients fell within this normal range indeed h B.M.R. were more closely clustered round the mean an were the preceding B M.R measured with the patient ake. Similarly most of the patients in the other oups did not show *much alteration* in B M R when ey went to sleep with the striking exception of the ervous' patients, in all of whom the reading dropped within the *normal* range

Fig. 3 shows the results obtained with amylobarbitone dium when the patient had been sufficiently sedated sleep through the procedure The cases were fewer t the trend was the same as after pentobarbitone dium: in most euthyroid patients the B M R. during ep was normal whereas in thyrotoxic patients it was gh and in myxœdema it was low In one patient the M.R. during sleep after oral amylobarbitone sodium s high but subsequently it was normal after intra nous pentobarbitone sodium which fact suggests that e patient was not really asleep after amylobarbitone dium

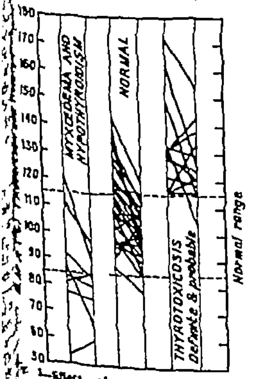

Fig. 3—Effect of oral amylobarbitone sodium on B.M.R. Only tests in which the patient was sleeping are included. Results expressed in the same way as in Fig. 2.

## Comments

We have come to regard the estimation of the B M R *during sleep* as eliminating one of the main sources of error in assessing thyroid function by the measurement of oxygen consumption We are satisfied that the B.M.R during sleep of euthyroid persons does not fall below the normal standards of Robertson and Reid (1952) and that of definitely hyperthyroid patients is above this normal range We believe that the patients must be really asleep at the time of the test, and that partial sedation is as likely to excite them as to calm them Heavy oral sedation is probably adequate in most cases but occasionally it may be necessary to use intravenous pentobarbitone sodium We are aware that ideally it should not be necessary to put patients to sleep to induce a basal state, but we gather that ours is not the only hospital where it has often proved extremely hard to obtain a reliable B M R with the patient awake

*When a* B M.R. *has been estimated during sleep it is* important to use standards referable to a truly basal state such as those of Robertson and Reid (1952) Only *for the Robertson and Reid standards* were the healthy people first given practice runs until two readings agreeing within 5% were attained A B M.R. expressed as a percentage of the age and sex mean value of these Robertson and Reid standards will be about 10% higher than when it is related to any of the older standards

We have had no untoward experiences with intravenous pentobarbitone sodium which acts slowly and is generally considered to be extremely safe We wish to emphasise *that the patients under the influence of pentobarbitone* sodium are asleep and not anæsthetised inasmuch as vigorous efforts can rouse them and their reflexes remain unaltered. The only serious disadvantage of the procedures we have described is that the patients remain drowsy and occasionally restless for the rest of the day The reliability of the results obtained probably justifies this inconvenience

### Summary

Intravenous pentobarbitone sodium was given to 73 patients for the estimation of the B M R during sleep

The B M.R. during sleep is abnormally high in thyro *toxic patients, within the normal range* in euthyroid and nervous patients, and low in myxœdema

Sleep was also induced with oral amylobarbitone sodium in 53 patients and rather similar results were obtained

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# RUPTURE OF LAPAROTOMY WOUNDS

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THE *incidence* of wound disruption or "burst abdomen" is undoubtedly higher than is generally realised Milbert (1935) found 20 cases of partial or complete disruption in 1500 laparotomies (1 3%) and Wolff (1950) reporting 45 cases in 1700 consecutive abdominal operations (2 6%) states that the incidence based on published reports is 0–3% These figures take no account of incisional hernia which may be regarded as bursts beneath an intact skin closure *discovered* usually after the discharge of the patient from hospital Romanis and Mitchiner (1937) *estimate* the incidence of incisional hernia at 4% hence the total incidence of wound dehiscence may be up to 7% of all abdominal incisions

I report here the results of an investigation made at a provincial hospital into the possible causes of wound disruption

### Method

A two page questionnaire was prepared, to be completed at the time of the resuture covering the patient's preoperative *condition*, operative details and findings at the time of the repair

TABLE I—EARLY BURSTS

| Age (yr) | Incision | Operation | Suture material | Tension sutures | Post-operative distension | Cough | Ambulant | Day of disruption | State of suture material |
|---|---|---|---|---|---|---|---|---|---|
| 52 | Paramedian | Appendicectomy | Catgut | Yes | | + | No | 4 | Broken |
| 64 | Midline | Gastrectomy | Catgut | Yes | | | No | 4 | Broken |
| 68 | Paramedian | Gastrectomy | Catgut | Yes | | + + | No | 5 | Broken |
| 60 | Paramedian | Gastrectomy | Catgut | Yes | | + | Yes | 7 | Broken |
| 70 | Kocher | Choledochostomy | Catgut | Yes | + | | No | 7 | Torn through tissues |
| 51 | Paramedian | Laparotomy | Catgut | Yes | | + | No record | 5 | Broken |
| 10 | Paramedian | Repair of ileum | Catgut | No | + | | No | 1 | Broken |
| 70 | Paramedian | Gastrectomy | Catgut and nylon | No | + | | No | 7 | Broken |
| 65 | Midline | Gastrectomy | Catgut | No | + | | Yes | 7 | Broken |
| 70 | Paramedian | Gastrojejunostomy | Catgut | Yes | + + + | | No | 6 | None found |
| 72 | Paramedian | Gastrojejunostomy | Catgut | No | | + + | No | 5 | Torn through tissues |
| 45 | Paramedian | Hysterectomy | Catgut | No | | + | No record | 7 | Broken |
| 73 | Paramedian | Gastrectomy | Catgut | Yes | | + | No | 3 | Broken |
| 73 | Paramedian | Abdominoperineal | Catgut | No | | | No | 3 | Broken |
| 63 | Paramedian | Repair of ventral hernia | Silk | No | | + | No | 5 | Torn through tissues |
| 41 | Paramedian | Cholecystectomy | Catgut | Yes | | | No | 1 | Broken |
| 64 | Paramedian | Abdominoperineal | Catgut and nylon | Yes | | | No record | 2 | Broken |
| 68 | Paramedian | Laparotomy | Catgut | Yes | | | No | 7 | Broken |

## Results

"Bursts" followed 28 of 2039 operations (1·4%). One questionnaire was completed inadequately, leaving 27 cases for analysis.

The cases fell into two main groups: an early group in which the disruption took place in the first seven days, and a late group in which the wound gave way on the ninth or a subsequent day. In the latter group every case showed either a low serum-protein level or a local condition of the wound (either hæmatoma or sepsis, or both) to account for delay in healing and consequent disruption when the suture material ceased to hold.

It is the early group, comprising 18 cases, to which particular attention is to be paid, for it is the surgeon's duty to ensure that his closure will withstand all strains put on it until sound healing has taken place. The nature of the strain is therefore really irrelevant to the issue, but in this connection one clinical observation is worth mentioning. When a conscious postoperative patient coughs, he does so with due care and support of his abdomen. In the theatre removal of an endotracheal tube, or aspiration of mucus through the tube, when the plane of anæsthesia is rapidly lightening can lead to most violent coughing in a still unconscious patient. The wound is unsupported, and the abdominal muscles can be seen standing out in powerful contraction. It may well be that some disruptions are thus initiated by breaking of the suture material or tearing out of sutures, and in fact 2 of the wounds did burst in twenty-four hours owing to broken catgut.

Of the 18 cases, the suture material was found broken in 14 and had torn through the tissues in 3 (and in 1 of the late group), and in the remaining case no trace of the catgut was found on the sixth day. The postoperative days on which abdominal viscera burst through the skin are shown in tables I and II. The burst is always accompanied by serous fluid, often bloodstained. In many cases similar fluid oozes from the wound for several days beforehand, indicating that the deeper layers have given way at this earlier date. So constant is this serou[s] discharge that its appearance presages either disruptio[n] of the wound or an incisional hernia.

## Discussion

*Nature of Suture Material*

Table I shows that in this series both catgut a nylon had broken, whereas there is no instance of s having done so. There is no record of the strength of th catgut used, but in most cases it would be no. 1 or no. 20 day chromic. Whatever the nature of the mater there is no doubt that it is sometimes faulty wh handed to the surgeon, either from age, repeated boili prolonged storage in phenol, or, in the case of catg by fraying on the broken glasss of the ampoule. It h been my custom for some time to attempt to break th suture material before use, and it is possible to do easily with disconcerting frequency. If a steady p in the surgeon's hands does not break it (nearly alwa one can do so with a sudden tug), the patient's abdomin muscles are unlikely to do so.

*Faulty Use of Material*

A double knot tied in catgut is unsafe. Experiment showed that such a knot can often be untied by a stead pull on the long end. Even three loops on the knot i not entirely safe, unless the short end is left at lea $^1/_4$ inch long, and this is still true if the first two loo form a reef knot. It is therefore wise to cut the sh end and to test the knot before proceeding with a co tinuous suture, so that any slipping under tension ca be observed and another suture substituted.

Other faults, which have been observed in severa hospitals, are attempting to close the abdomen wit inadequate relaxation, leading inevitably to tears i the tissues during the procedure, and seizing the materia with the needle-holder to draw the suture tight (such crushing must weaken the material and predispose t breaking).

TABLE II—LATE BURSTS

| Age (yr) | Incision | Operation | Ambulant | Post operative distension | Cough | Wound hæmatoma | Wound sepsis | Serum protein level (g per 100 ml) | Day of burst |
|---|---|---|---|---|---|---|---|---|---|
| 72 | Paramedian | Laparotomy | No | + + + | | No | Yes | 6·8 | 12 |
| 48 | | Laparotomy | No | + | | No | Yes | 4·7 | 13 |
| 72 | | Ileo transverse colostomy | No record | | + | No | Yes | 5·5 | 10 |
| 55 | ,, | Gastrojejunostomy | Yes | | + | No | No | 5·7 | 11 |
| 35 | | Resection of jejunum | No record | | | No | Yes | 3·9 | 9 |
| 76 | ,, | Gastrojejunostomy | No record | + | + | No | Yes | 5·8 | 11 |
| 73 | | Laparotomy | No | | | No | Yes | 6·0 | 13 |
| 71 | | Transplantation of ureters | No | + | | Yes | No | 6·1 | 10 |
| 64 | | Resection of colon | No | + | | No | Yes | 5·4 | 12 |

*Method of Suture*

“The fatter the patient the thinner the peritoneum” is almost invariably true, and obesity has long been cited as a factor in wound disruption It is clearly unwise in such cases, when sutures tear through the tissues so easily to rely on a continuous suture alone

The weakness of an investigation such as this which ollects data after the event, is the lack of controls. The record of the method of suture depends largely on he memory of the house-surgeon and the consistency of he surgeon concerned in his technique of closure Again in the absence of a record of the frequency with which arious methods were used, one cannot draw conclusions bout their relative efficiency Nevertheless the fact at tension sutures had been used in 17 of these 27 ruptions casts doubt on their usefulness Moreover 22 cases simple continuous sutures had been used for oth layers which fact, with 15 cases of breakage of he material, confirms the impression that this method suture is not without risk

*mbulation*

Of the 27 patients 17 had not been out of bed at the me of the disruption 4 were ambulant and in 6 there no record. These figures, though small confirm the inion of Leithauser (1943) and Nelson (1944) that rly ambulation has little effect on the incidence of hiscence

*cision*

In the absence of controls no conclusion can be drawn the relative merits of the various incisions in common

In this series 16 disruptions were through upper dominal incisions (1 Kocher 2 midline and 13 para dian) and 8 through lower abdominal incisions (all amedian) This point is discussed by Wolff (1950) o worked out the disruption rate for each of the mmon incisions, and concluded that the small differ es for site and type of incision have no statistical nificance He suggests that increased intra abdominal ssure, which theoretically should be exerted equally all directions, is of more importance than the direction muscle pull in disrupting the wound The importance increased intra abdominal pressure cannot be doubted d in this series most of the patients had postoperative tension or cough.

*rtality*

In this series the disruption was considered to have en responsible for the deaths of 5 patients: from alytic ileus in 1 and from chest complications in 4.

## Summary

The results of an investigation into the cause of burst abdomen’ are recorded

The cases fall naturally into early and late groups

Many of the early group are perhaps avoidable

My thanks are due to the surgeons of the Brighton and ewes Hospital Group for access to their patients; and articularly to Mr H J McCurrich and Mr K. W Powell, ho instigated the work for their help and constant interest

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Dr Weir Mitchell tells of once sending a colleague o see an old Quaker lady Next time he saw her she said o him ‘Never send that man to see me again. Thee knowest I do not like to have my feelings poulticed’ —Prof JOSEPH FLETCHER, *Morals and Medicine* London 1955; p 34

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# INFECTION WITH CRYPTOCOCCUS NEOFORMANS IN MAN

## REPORT OF TWO CASES

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SINCE the original publication of Busse (1894) and Buschke (1895) of a case of human torulosis * there have been numerous reports of this condition particularly from the United States and Australia Collins et al (1951) review 241 collected cases to which they add 2 of their own In contrast to the frequency of this disease in other countries its incidence in Great Britain appears to be low for Symmers (1953), who reported 2 cases could find only 8 cases previously published in this country

Torulosis has an insidious onset and a protracted course, most commonly declares itself when the central nervous system has become affected, and then usually progresses to a fatal termination within one to four months In a few cases reviewed by Linden and Steffen (1954) the infecting agent appears to have remained localised at the site of entry which is thought to be most often the lung

In view of the paucity of symptoms reported in pulmonary cryptococcosis and the tendency of cryptococcal infection to simulate other-diseases, it is not unlikely that it may be either overlooked or wrongly diagnosed Thus it may be more common than appears from the number of published cases

For this reason we report our 2 cases The first was originally diagnosed as Hodgkin's disease until terminal meningitis revealed the true nature of the illness and the 2nd case was recognised as pulmonary cryptococcosis only after resection

### Case reports

Case 1.—A man aged 27 was discharged from the Army in 1947 with the diagnosis of Hodgkin's disease, which had been established by biopsy of a cervical lymph node Unfortunately the slide made from this biopsy specimen could not be traced. The patient subsequently received deep X ray treatment for three years. He was admitted on Aug 21 1950 to the North West Branch Royal Free Hospital, with three months history of loss of use of his right hand and three weeks history of intense headache giddiness, muscular weakness and vomiting He had some memory defect and delusions and had lately developed diplopia.

*On admission* he was lethargic and his speech was slurred He had severe neck rigidity a positive Brudzinski's sign bilateral papilloedema right external rectus palsy and left lower facial weakness His tendon reflexes were diminished and he had general weakness of all his limbs.

*Pathological Investigations*—The cerebrospinal fluid (c.s.f.) was under a pressure of more than 300 mm. and contained 40 cells per c.mm. (lymphocytes 88%) protein 90 mg per 100 ml. an excess of globulin chlorides 670 mg per 100 ml and sugar 28 mg per 100 ml. A gram-stained film revealed numerous yeast-like bodies, which were later identified as *Cryptococcus neoformans* Culture on blood-agar yielded a visible growth of this organism after twenty four hours A white cell count showed 14,400 leucocytes per c mm (polymorphs 87%, lymphocytes 6%, monocytes 7%) The urine contained a trace of albumin and a few leucocytes, culture produced a few colonies of enterococci

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* In accordance with modern terminology the name *Cryptococcus neoformans* has been adopted for the organism [illegible] this condition

*Treatment and Progress*—The patient received daily intra thecal streptomycin 0 1 g and penicillin 10,000 units, intra muscular streptomycin 1 g and penicillin 3 mega units, and ‘Sulphatriad’ 8 g by mouth There was no change in his condition, and his C S F continued to harbour numerous cryptococci His temperature, which had been normal on admission, gradually rose to 103°F, and he died in coma on Aug 28, 1950

*Necropsy Findings*—The C S F was turbid, and the surface of the brain showed flattening of convolutions, there were no macroscopic gelatinous granulations in or beneath the pia arachnoid The *lungs* had undergone much post mortem autolysis, but there was evidence of incipient suppurative bronchopneumonia in both lower lobes The *abdominal glands* in the root of the mesentery and the para aortic and cœliac groups of glands were moderately enlarged The *liver* resembled hepar lobatum with coarse scarring, its cut surface was mottled and pale The *spleen* was enlarged to about four times its normal size, and section revealed scattered nodules of soft whitish tissue up to 1 5 cm in diameter The left *psoas major muscle* contained a mass of soft whitish tissue, which was about 7 cm in diameter and had eroded the transverse process of the third lumbar vertebra The *axillary and inguinal glands* were slightly enlarged and firm, their cut surface did not reveal any gross abnormality

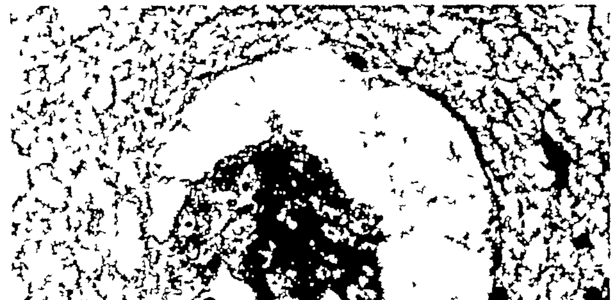


**Fig 1—Case 1 : cortical " cyst " of brain containing numerous cryptococci (Hæmatoxylin and eosin × 450 )**

*Histology*—The *meninges* showed a sparse cellular infiltrate consisting of lymphocytes, plasma cells, macrophages, and a few multinucleated giant-cells, with numerous cryptococci lying freely between these cells or being phagocytosed by macrophages and giant cells The inflammatory infiltration extended along the perivascular spaces into the cortex, which showed a few small cystic areas stuffed with cryptococci and a few inflammatory cells (fig 1) The *spleen* (fig 2) was engorged and showed well defined and sharply demarcated areas of infiltration with pleomorphic tissue resembling that found in Hodgkin's disease and composed mainly of lymphocytes and large hyperchromatic cells with giant indented or lob nuclei, occasionally a binucleated cell of the Reed-Sternb type was seen No eosinophils were present A simil type of tissue was found in the para aortic, mediastin and supraclavicular *lymph glands*, in the last two viving only as small scattered areas amidst dense po irradiation fibrosis The mass in the *psoas major mu* (fig 3) again was composed of similar tissue, but here t large hyperchromatic cells were more numerous and t appearances tended to resemble those of Hodgkin sarco The *liver* showed fibrous thickening of the capsule and intersected by broad bands of fibrous tissue in which a few small collections of lymphocytes were seen. *kidneys* contained small areas of lymphocytic infiltration the cortex, in which occasionally cryptococci were foun No cryptococci were seen in the tissue resembling that Hodgkin's disease in the spleen, lymph glands, and pso nor were they found in the liver

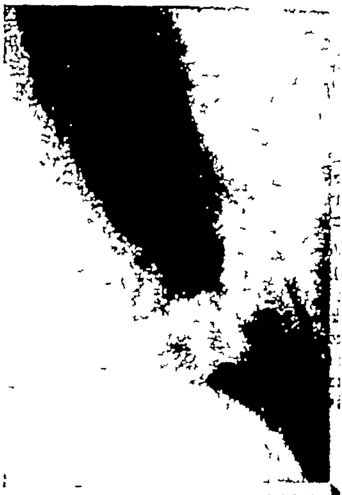
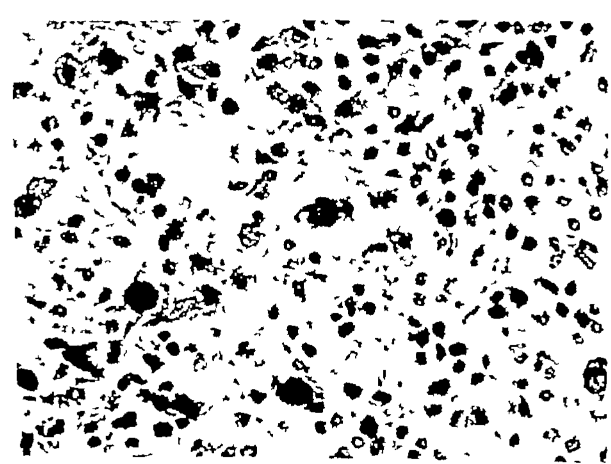


**Fig 4—Case 2 tomogram of left l showing several cavities at base.**

*Description of Organism*—Microscopically the organ displayed the characteristic appearances of *Cryptococ neoformans* round or ovoid bodies showing budding, a staining (in sections) bright red with mucicarmine and wi periodic acid Schiff stain Each body was surrounded by unstained capsule, which could be seen in preparations the C S F deposit stained with nigrosin The organism gr well on agar and Sabouraud's medium both at roo temperature and at 37°C The colonies were smooth, ent greyish, and of buttery consistence, later becoming muc No mycelium was formed in culture, The organism ferment glucose and sucrose, with the formation of acid an Mannite, dulcitol, lactose, maltose, sorbitol, and mosite w not split Liquefaction of gelatin was not observed dur



**1 : splenic tissue resembling lesion of Hodgkin's disease. (Hæmatoxylin and eosin × 450 )**

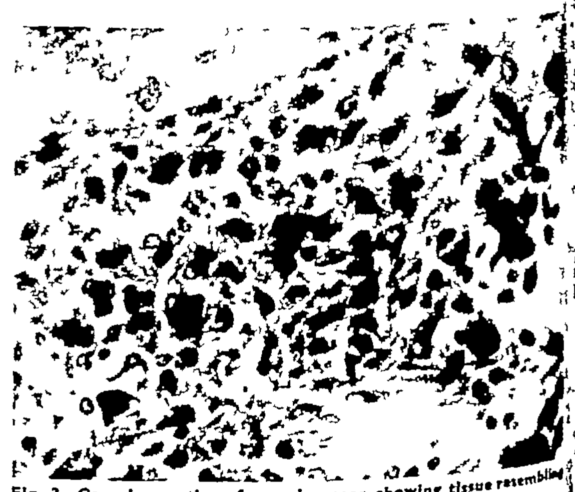
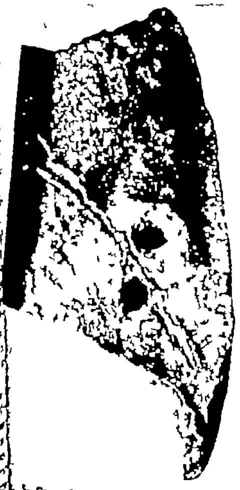


**Fig 3—Case 1 : section of mass in psoas showing tissue resembling Hodgkin sarcoma. (Hæmatoxylin and eosin × 450 )**

inoculation for four weeks. In routine sensitivity tests with impregnated discs the organism was resistant to sulphathiazole penicillin, streptomycin chloromycetin aureomycin, oxytetracycline and polymyxin. It was virulent for both mice and guineapigs A mouse injected intraperitoneally with 0·25 ml. of a heavy suspension from a Sabouraud culture died seven days later cryptococci were recovered from its peritoneum and brain Similarly a guineapig injected intraperitoneally with 1 ml. of C.S.F. died fourty four days later from generalised infection cryptococci were present in sections of brain, spleen liver kidney lung, and inguinal and other lymph-glands.

Case 2.—A male shorthand typist aged 32 was admitted on Jan. 4, 1954 to the thoracic unit of St Charles Hospital for investigation of a lesion at the base of his left lung which had been found in August 1953 by routine mass miniature radiography He complained of some pain in the left side of his chest which was not pleuritic in type He had no cough or other symptoms suggesting a chest infection A course of penicillin given before his admission had not changed his X ray shadows. He had served in South Africa Italy and France in the 1939–45 war and had been discharged from the Royal Air Force in 1946 because of loss of sight in his right eye In 1949 the left eye also became affected. He was investigated at two hospitals and Eales's disease was diagnosed There was no evidence of tuberculosis and a Mantoux test was negative At one time retinoscopy was said to have revealed "perivascular choroidal tubercles," and on the assumption that his condition was tuberculous the patient was given a prolonged course of streptomycin (total 200 g.) followed by streptomycin in combination with p-aminosalicylic acid and later isoniazid His eye condition however did not improve after this treatment.


5—Case 2: left basal segments of lung, showing infiltration and cavitation.

On admission his general condition was good He was ...rtal, and there were no abnormal chest signs. He was ...lly blind in his right eye and the visual acuity of the ...ye was 6/12. Radiography of his chest (fig 4) revealed ...led opacities with thick walled cavities in the left lower ... The patient did not produce any sputum and nine ...ngeal swab cultures as well as a culture of bronchial ...ings, did not produce tubercle bacilli. The erythrocyte ...mentation rate (Westergren) was 7 mm in the first hour ...Mantoux test was positive in a dilution of 1 10 000 A ...d-count was normal, and the Wassermann reaction and ...hn test were negative

Treatment and Progress.—Despite the negative results of ...m the lesion was thought to be tuberculous and after ...en preparatory course of streptomycin and p aminosalicylic ...e and a left basal segmental resection was done by one ...s (A. R. M.) on Jan 15, 1954 The patient made an ...ntful recovery and was discharged from hospital on ...h 13, 1954

Operation Specimen (fig 5).—The anterior basal segment ...ained two large subpleural greenish yellow nodules. Further ...ll nodules were palpable in the deeper parts of the basal ...ments. On section the cut surface revealed nodular areas ...reyish yellow infiltration varying in diameter from a few ...llimetres to 2 cm. The larger nodules tended to coalesce ...d showed central cavitation There was some fibrosis at the periphery of the lesions and a small area of collapse in the middle basal segment with occlusion of the corresponding subsegmental bronchus Microscopy of the nodular areas (fig 6) showed that the lung parenchyma had been superseded by granulomatous tissue composed of numerous giant-cells of foreign body type macrophages, lymphocytes and fibroblasts. The larger lesions showed central necrosis and cavitation surrounded by fibrous tissue At the periphery of the nodules the alveoli had thickened walls and contained in their lumen collections of giant-cells and macrophages Throughout the lesion these cells were stuffed with highly refractile spheroid bodies (fig 7) which were 5–10 μ in diameter and were surrounded by a halo 7–17 μ in diameter With hæmatoxylin and eosin their outline was only faintly stained but they were easily recognised by their high refractility In sections stained with periodic acid Schiff stain they appeared faintly pink with a distinct red outline and an occasional bright red dot in their centre or at their periphery The halo remained unstained These bodies were numerous throughout the lesion and were also found lying freely between the granuloma cells. They were shown to Dr R W Riddell of the department of bacteriology Brompton Hospital who confirmed the diagnosis of *Cryptococcus neoformans* Unfortunately the nature of this lesion was only realised on histological examination of the excised lung Attempts to isolate the organism from the formalin fixed tissue three weeks after operation were unsuccessful. Sections of parabronchial lymph glands from the excised specimen did not reveal any granulomatous tissue

*Follow up.*—The patient has remained well for thirteen months after operation Repeated postoperative laryngeal swabs and urine cultures for cryptococci have been negative

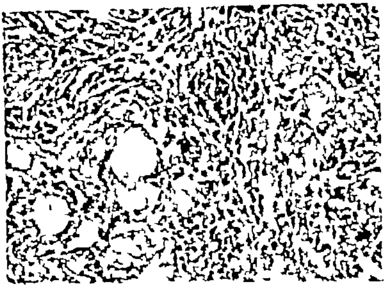


Fig 6—Case 2: section of lung, showing granulomatous tissue with giant cells containing cryptococci. (Hæmatoxylin and eosin. × 170)

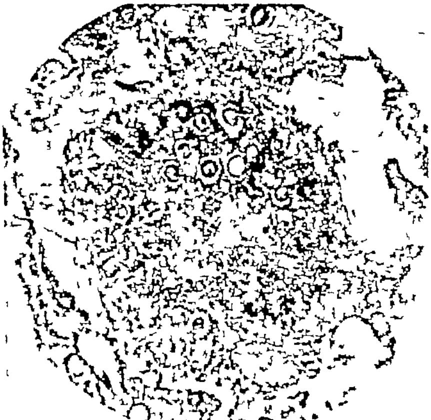


Fig 7—Case 2: Cryptococci in giant-cell from granuloma of lung (Periodic acid Schiff × 750.)

and radiography of the lungs and skeleton has revealed no abnormality Lumbar puncture was not done, because it was felt that it might possibly be harmful to the patient

## Discussion

Cases 1 and 2 illustrate the varied clinical manifestations by which cryptococcal infection may declare itself for the first time The association with lesions resembling those of Hodgkin's disease, seen in our first patient, has been reported before Cox and Tolhurst (1946), in their review of 100 cases of torulosis, estimate its frequency to be at least 5%, whereas Collins et al (1951) found it in 11 of the 243 cases reviewed by them This frequency is too high to be fortuitous and suggests either an increased liability to fungus infection of patients with Hodgkin's disease or a causal relationship between the fungus and the lesions resembling those of Hodgkin's disease Our failure to find cryptococci in these lesions does not exclude the second possibility, since in most of the published cases cryptococci were either not demonstrable in the tissue resembling that of Hodgkin's disease or were present only in very small numbers If the glandular enlargement which led to the diagnosis of Hodgkin's disease in case 1 is taken as the earliest manifestation of his infection, his illness lasted at least four years The diagnosis of his terminal meningitis did not offer any difficulties, because cryptococci were easily demonstrated both in direct films and by culture of the C S F

The first manifestation of cryptococcal infection in case 2 was probably the eye lesion which led to his loss of vision Cryptococcal chorioretinitis leading to extensive intraocular destruction has been reported so far in 4 cases, reviewed by Wager and Calhoun (1954) The underlying pathological lesions are necrotising granulomata in which cryptococci have been demonstrated both by culture (Weiss et al 1948) and in stained sections The perivascular choroidal "tubercles" reported in case 2 may well have been such granulomata This assumption receives further support from the negative result of the Mantoux test at the time these eye lesions were seen and from the absence of pulmonary tuberculosis It therefore seems that he became infected before his discharge from the Royal Air Force and at least seven years before his lung condition was diagnosed The chance finding of this extensive lesion by mass miniature radiography emphasises the insidiousness of cryptococcal infection Since it was thought to be tuberculous and its nature was only recognised after histological examination of the operation specimen, the diagnosis of cryptococcal infection is based entirely on the morphological and tinctorial appearances of the organism in sections We believe, however, that these were definite enough to justify our diagnosis

Although case 2 has so far remained well for thirteen months after his operation, the long term outlook as regards his freedom from further evidence of infection is uncertain "Cures" of pulmonary cryptococcosis by excision of the affected lung have been reported and are reviewed by Corpe and Parr (1954), but, in view of the protracted course of this infection, the period of observation in many of these cases cannot be considered adequate Even follow-up periods of four years (Baker 1952 case 3) and five and a half years (Froio and Bailey 1949) after lobectomy fall within the range of latency observed in torulosis Unfortunately there is not yet a chemotherapeutic agent of established value against cryptococci which could be used as a supplement to surgical measures

## Summary

2 cases of cryptococcal infection are reported

Case 1, was regarded for four years as one of Hodgkin's disease until the true diagnosis was revealed by terminal meningitis and the demonstration of *Cryptococcus neo*
s in films and cultures of the C S F At necropsy
ding those of Hodgkin's disease were found in the spleen, some lymph-glands, and the left psoas major muscle

Case 2 presented as localised pulmonary cryptococcosis, which was treated by segmental resection Seven years previously he had developed chorioretinitis, which led to blindness and, we believe, was caused also by cryptococci.

We wish to thank Dr W Gunn and Mr C A Jackson, F.R.C.S., for permission to publish these cases, and Dr Ridde for help in identifying the organism in case 2 The origin isolation of the organism from the C S F, of case 1 was th work of the late Dr George Stephen Acknowledgments ar also due to Mr Sheppard and Mr Kemp for the photograph

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# PROLONGED JAUNDICE WITH UNIDENTIFIED PIGMENT IN LIVER CELL

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A NEW liver disease was described by Dubin a Johnson (1954), who reported 12 cases of chronic intermittent jaundice which affected young people a was usually manifested by pain in the upper rig abdominal quandrant, mild jaundice, fatigue, slig enlargement of the liver, and dark urine The jaundi lasted from a few months to several years, fluctuated i intensity, and was aggravated by intercurrent disea The prognosis was very good Laboratory examinatio revealed bilirubinæmia, a raised direct van den Ber reaction, retention of 10–30% of bromsulphalein, ceph flocculation and thymol turbidity often positive, bilirubinuria The gall-bladder did not show up cholecystography Liver biopsy revealed always norm hepatic structure without any signs of either inflamma tion or fibrosis A coarsely granular, amorphous, greenis brown pigment was found in the central cells of th lobules Macroscopically the liver was dark gree slate grey, or black Dubin and Johnson could no identify the pigment, which shared some chemic properties with ceroid and lipochrome pigments

These cases differ from those reported by Gilber and Lereboullet (1901), Rozendaal et al (1935), an Dameshek and Singer (1941) as familial non hæmolyti jaundice or constitutional hepatic dysfunction, in whi the bilirubin was of the indirect type, there was n bilirubinuria, the liver was not enlarged, liver functio was usually normal in spite of jaundice, and any pigmen present was finely granular The cases reported b Dubin and Johnson could readily be distinguished fro hæmolytic, obstructive, and infectious jaundice (See als *Lancet* 1954 )

We report here a case which came under ou observation

## Case-report

A married woman, aged 28, of German origin was admitte to this hospital in June, 1954, with six years history o ndice Nothing relevant was found in her past history and her family history Six years ago, when she noticed the ndice for the first time her only other complaint was ue epigastric pain After two months the jaundice became intense but did not disappear completely The patient well all the time During the following years the jaundice tuated in intensity but was always present A month ore admission she was found on a routine gynæcological mination, to be in the sixth month of pregnancy and ause of the jaundice was directed to our ward

*On examination* she was well nourished and in good general lth. Her scleræ and skin were yellowish and her liver ended to 4 cm. below the costal margin. The size of her rus was consistent with seven months pregnancy Nothing normal was found elsewhere

*Investigations* —Examination of the patient's blood showed 9·9 g per 100 ml. leucocytes 5300 per c.mm (differential nt normal); reticulocytes 1%; erythrocyte-sedimentation e (E.S.R.) 20 mm in 1st hr (Westergren); serum protein g per 100 ml (serum-albumin 4·6 g per 100 ml serum bulin 2·8 g per 100 ml.) serum cholesterol 202 mg r 100 ml., serum-cholesterol esters 132 mg per 100 ml rum-alkaline phosphatase 1·5 Bodansky units serum irubin 3·0 mg per 100 ml. (direct 1·8 mg per 100 ml direct 1·2 mg per 100 ml); prothrombin time 100%; mol flocculation negative thymol turbidity 6–7 Kahn t negative The urine contained bilirubin and more urobinogen than usual In blood-smears no spherocytes were en. The fragility test gave normal values, the Coombs t was negative and no cold agglutinins were found No a, parasites, or amœbæ were found in the stools. The fæcal retion of stercobilinogen was 115 mg in twenty-four urs. The gall bladder did not fill after a double dose of al dye. Fluoroscopy of the chest was negative

*Progress* —During three weeks in hospital the patient's ndition did not change and the laboratory findings remained nstant Chronic hepatitis was diagnosed, and the patient s advised to come back for further investigation after the rth of her child.

*Readmission* —In November 1954 the patient was admitted to the hospital for further examination Two eks previously she had been delivered of a child that died on afterwards. The cause of death was not definitely ablished

*On examination* the patient's condition was essentially same as on the previous admission She felt well and apyrexial; her liver extended 4 cm. below the costal rgin, and her scleræ and skin were yellow

*Investigations* —Examination of her blood showed Hb 3 g per 100 ml; leucocytes 5400 per c.mm E.S.R mm. in 1st hr (Westergren) serum protein level normal rum-alkaline phosphatase 1·35 Bodansky units; serum rubin 4·8 mg per 100 ml. (direct bilirubin 3·6 mg per ml. and indirect 1·2 mg per 100 ml); thymol turbidity 6; thymol flocculation negative bromsulphalein retention after 45 minutes; plasma iron 113 µg per 100 ml. gall bladder did not fill when dye was given by mouth. er biopsy showed a normal parenchyma without distortion structure No signs of cellular infiltration and fibrosis re noted. Many liver cells, mostly in the centres of lobules tained numerous granules of brownish pigment which ve a negative reaction for bile and iron The bile-ducts re not distended. The biopsy specimen was dark green

*Progress* —The patient was discharged from hospital hout a clear-cut diagnosis and was advised to eat plenty proteins and vitamins

*Readmission.*—In January 1955 the patient was admitted a third time At home she had felt well except for a ll constant pain in the right hypochondrium

*On examination* she was jaundiced her liver was of the me size as before and enlargement of her spleen was doubtful. Hepatic function, bromsulphalein retention (29%) bilirubin, hymol turbidity and flocculation serum alkaline phosatase serum proteins, and liver biopsy showed no change The gall bladder still did not fill with dye and radiography f the stomach was normal On two occasions there was tention of water after drinking 1200 ml as in diseases f the hepatic parenchyma

## Comments

The present case closely resembles those described by Dubin and Johnson (1954) and Sprinz and Nelson (1954) When the patient was first admitted with six years' history of jaundice, we considered chronic hepatitis or incomplete obstruction of bile-ducts as a possible diagnosis, but liver biopsy revealed a perfectly normal structure the only abnormality being a brownish coarse pigmentation of the liver cells Clinical and laboratory examinations did not show any signs of obstruction of the bile-ducts or hæmolysis There was no history of peptic ulcer colitis, or other chronic gastro-intestinal disturbance Despite the prolonged jaundice the patient was in excellent general health

We are inclined to agree with Dubin and Johnson (1954) that the disease is a new clinicopathological entity and probably represents an inborn error of metabolism. It seems that bilirubin, bromsulphalein, the pigment that accumulates in the liver cells and the dyes used in cholecystography cannot be properly excreted

Since the disease does not seem to inconvenience the patient much, and the prognosis appears to be good its recognition is of great importance Before the publication of the paper by Dubin and Johnson we were considering exploratory laparotomy probably many such patients have undergone operation in the past This disease can easily be diagnosed by liver biopsy

## Summary

A case is reported of a new liver disease first described by Dubin and Johnson (1954)

The patient was a young woman who for six years had had continuous jaundice without its affecting her excellent general health

Clinical examination revealed nothing abnormal except jaundice and slight enlargement of the liver Laboratory examination revealed a raised serum bilirubin level mainly of the direct type, and increased retention of bromsulphalein The gall bladder did not fill with opaque dye

The disease was diagnosed by liver biopsy which revealed a characteristic brownish pigment in the liver cells

We wish to thank Dr H Spitz, our pathologist whose coöperation made this work possible

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# ACUTE YELLOW PHOSPHORUS POISONING
## WITH RECOVERY

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RAT POISON is freely available to the general public and may contain appreciable amounts of inorganic yellow phosphorus Cases of phosphorus poisoning although infrequent occur from time to time either with suicidal intent or more rarely accidentally

We report here a case in which recovery followed the ingestion of about 500 mg of yellow phosphorus. This quantity must be considered highly lethal; Sollmann (1948) states that the fatal dose is generally about 100 mg The variability of the clinical picture is well exemplified in the present case.

## Case report

A widow aged 71 was admitted on the evening (day 1) having taken about 500 mg of yellow the form of Rodine a rat poison con

FINDINGS IN ACUTE YELLOW PHOSPHORUS POISONING

| Day | 4 | 5 | 7 | 9 | 10 | 15 | 16 | 22 | 37 | 42 |
|---|---|---|---|---|---|---|---|---|---|---|
| Blood urea level (mg per 100 ml) | | 122·0 | | 130·0 | | | 58·0 | 46·0 | 30·0* | |
| Serum sodium level (mg per 100 ml) | | 275·0 | 285·0 | 280·0 | | | 315·0 | 320·0 | 325·0 | |
| Serum potassium level | | 17·5 | 18·0 | | | | 13·5 | 23·0 | 18·0 | |
| Plasma-chloride level (mg per 100 ml) | | 445·0 | 421·0 | | | | 538·0 | 620·0 | 573·0 | |
| Plasma bicarbonate level (vols $CO_2$ %) | | | | | | | 68·0 | 53·0 | 53·0 | |
| Serum phosphorus level (mg per 100 ml) | | | | 3·1 | | | 2·4 | 3·3 | 3·2 | |
| Serum-calcium level (mg per 100 ml) | | | 5·8 | 6·2 | | | 6·6 | 8·3 | 9·5 | |
| Serum bilirubin level (mg per 100 ml) | 10·0 | | 16·0 | | | 16·0 | | 2·6 | 1·4 | 0·7 |
| A/G ratio | 4·3/2·3 | | 3·6/1·5 | | | 2·1/2·5 | | 2·3/3·0 | 2·0/3·4 | |
| Thymol turbidity (units) | 1·2 | | 1·0 | | | 2·5 | | 1·4 | 2·3 | |
| Alkaline phosphatase (K A units) | 19·0 | | | | | 26·0 | | 31·0 | 19·0 | |
| Prothrombin (%) | | | 23·0 | | | | 70·0 | | 100·0 | |
| Hb % (Haldane) | 72·0 | | | | 76·0 | | | 38·0 | 76·0 | 80·0 |

* Urea clearance 63% of average normal

element For some months previously she had become increasingly depressed when she was left alone in her house for long periods, and at noon on the day of admission she consumed the dose spread on a slice of bread and butter Eight hours later she arrived at the hospital having vomited once at home

*On admission* her condition gave rise to no anxiety She was alert and coöperative, with regular pulse, pulse rate 100, blood pressure 135/90 mm Hg and temperature 98°F There was no evidence of icterus or of petechial hæmorrhages in the skin The lungs and cardiovascular and central nervous systems were essentially within normal limits, apart from some thickening of the peripheral vessels The abdomen exhibited a large incisional hernia (cholecystectomy in 1952) through which the liver was just palpable below the right costal margin No other viscera were palpable The urine contained no albumin, sugar, or bile pigments

*Treatment and Progress* —The stomach was washed out with copious amounts of water, and magnesium sulphate was put down the stomach tube (unfortunately the gastric return was not available for inspection), and after this the patient spent a restful night

*Day 2* —The patient remained well and took a full diet There was no further vomiting, and there was no evidence of icterus

*Day 3* —In the evening the patient was first noticed to be faintly jaundiced, although making no complaints

*Day 4* —Her condition rapidly deteriorated, and by 8 A M she was semi stuporose Obvious icterus was present, the skin cold and pale, the pulse impalpable, and the blood pressure non recordable The liver edge was now easily palpable through the incisional hernia about two finger breadths below the costal margin and tender The urine was scanty and loaded with albumin and bile pigments Delayed phosphorus poisoning with acute hepatic and circulatory failure was diagnosed A 5% dextrose infusion was set up and l noradrenaline 4 mg per litre was added to the drip, which was adjusted to maintain the systolic blood pressure between 100 and 120 mm Hg There was a most gratifying response, the radial pulse became palpable, and the blood pressure rose rapidly Intramuscular penicillin 500,000 units was given six hourly Despite the improvement in her peripheral circulation the patient relapsed into deep coma, and the depth of icterus increased

*Day 5* —Her condition continued to deteriorate, the jaundice became deeper, and the liver had enlarged to the level of the umbilicus Generalised coarse muscle fasciculation was observed although Chvostek's and Trousseau's signs were negative, and the plantar responses became extensor Parenteral vitamin therapy was started, and a "vitamin cocktail" was made up containing the following substances in a pint of glucose saline solution

| | |
|---|---|
| Aneurine | 50 mg |
| Nicotinamide | 150 mg |
| Riboflavine | 30 mg |
| Vitamin $B_{12}$ | 200 µg |
| Vitamin K | 200 mg |

A pint of this infusion was given daily In view of Walshe's (1953) suggestion that glutamic acid should be used in the treatment of hepatic coma, treatment was started with sodium glutamate two pints daily (sodium glutamate 23 g in a pint of 5% dextrose) The noradrenaline drip was also continued, ing amounts being required to maintain the blood

*Day 7* —The patient remained in deep coma 10% calcium gluconate was given to raise the low serum calcium level (see table)

*Day 8* —Some improvement in the patient's general condition was noted, and it was now possible to reduce the amount of noradrenaline without a fall in the blood pressure

*Day 9* —The degree of coma was appreciably lighter, and the liver was thought to be decreasing The noradrenaline drip was discontinued

*Day 11* —The patient could obey simple commands and take fluids by mouth *Intravenous therapy* was therefore discontinued

*Day 15* —The patient was now fully coöperative, the jaundice was appreciably less, and the liver had decreased further and was much less tender A high protein high carbohydrate diet was instituted with added 'Casilan,' vitamin supplements and methionine 1 g t d s

*Day 16* —Potassium chloride 2 g t d s was given by mouth to correct the low serum potassium level (see table)

*Day 22* —During the course of her illness the patient had become progressively anæmic, and in view of a hæmoglobin level of 38% (Haldane) she was transfused with two pints packed red cells

*Further Progress* —From this time onwards she made steady progress, her blood biochemistry returned to normal and the serum bilirubin level fell to within normal limits (see table) Apart from a troublesome pressure sore she was symptom free and said she had not felt so well for many years

## Discussion

Phosphorus occurs in two forms (1) the red amorphous variety, which is stable, insoluble, non absorbable and therefore for practical purposes non toxic when taken by mouth, and (2) yellow phosphorus, which is relatively unstable, soluble in fats and bile, and highly toxic The minimal lethal dose of ingested yellow phosphorus is 50 mg (Sollmann 1948), but as little as 15 mg of it may cause untoward symptoms Díaz Rivera et al (1950), however, reported recovery after the ingestion of 780 mg Previously survival after taking 200–400 mg was rare, and no survival had been reported after the ingestion of more than 400 mg (Bayne et al 1952)

Yellow phosphorus is a powerful protoplasmic poison producing its main effects on liver, kidneys, heart, and brain Impaired glycogenesis leads to depletion of liver glycogen and is followed by fatty infiltration of liver, kidneys, heart, and other organs Liver-biopsy specimens have presented the appearances of periportal fibrosis in the recovery phase (La Due et al 1944)

The typical picture of phosphorus poisoning falls into two distinct stages separated by a variable interval The first stage is one of gastro intestinal irritation, coming on within a few hours, and is characterised by thirst, nausea, vomiting, hæmatemesis, "garlic" eructations, and epigastric discomfort This stage usually lasts about twenty four hours and is followed by a period of apparent well-being—the latent period—lasting from a few hours to a few days, the length being conditioned by the rate of absorption of the phosphorus The second or systemic stage is characterised by nausea, vomiting, abdominal pain, icterus a tender palpable liver, hæmorrhages peripheral circulatory collapse, oliguria, coma, and death and depends on hepatic renal and cardiac failure

Deviations from the above are emphasised by Diaz Rivera et al (1950) in that patients who have consumed large amounts of phosphorus may die within the first twelve hours from peripheral circulatory collapse, and indeed the great majority of patients may die before the appearance of a clear-cut picture of hepatic damage

The appreciaton of the latent period by the physician is of prime importance because it may lead to a false sense of security the patient being discharged from hospital before the onset of the systemic stage, as in the case reported by Wechsler and Wechsler (1951)

The experience of Diaz Rivera et al (1950) in 56 cases suggests that the present case had many grave prognostic features a fairly considerable dose of poison minimal emesis, considerable delay before gastric lavage was instituted and especially the onset of the systemic stage with peripheral circulatory collapse and non recordable blood pressure This last feature is usually accepted as an indication of impending death By contrast encouraging features were the facts that the phosphorus was contained in a solid vehicle and that there was a long delay before the onset of the systemic stage.

All workers are agreed that the treatment of the peripheral circulatory collapse in this condition is most unsatisfactory Diaz Rivera et al (1950) state that the signs of shock early in the course of the disease is one of the most important therapeutic problems since the physician is helpless from the start ' In the light of this statement the response and maintenance of our patient s blood pressure by noradrenaline for six days must be considered most satisfactory, and it therefore seems that, with noradrenaline now generally available further improvement in the prognosis of yellow phosphorus poisoning may be anticipated The mortality in the Puerto Rico series of Diaz Rivera et al (1950) was 48% a large proportion of the fatal cases showing the "shock syndrome ' We feel that treatment with noradrenaline would have lowered this encouraging figure

The treatment of acute hepatic necrosis in the systemic stage does not appear to differ from the regime suggested by Latner (1950) The use of glutamic acid may be worthy of further trial but we were not impressed by its effect in the present case

Of prime importance however is therapy directed to the elimination of the phosphorus before it is absorbed This should include thorough gastric lavage with 1:1000 solution of potassium permanganate to oxidise the phosphorus to phosphates followed by the administration of 200 ml of mineral oil—e.g , liquid paraffin—which is a good solvent of phosphorus helps to prevent its absorption, and hastens its elimination

## Summary

A case of yellow phosphorus poisoning with recovery after the ingestion of about 500 mg is recorded

The use of noradrenaline in the treatment of peripheral circulatory collapse in this condition and the importance of early therapy are emphasised

We wish to thank Dr N Kletts for permission to publish this case and for his helpful criticism and advice

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# PURE RED-CELL APLASIA SUCCESSFULLY TREATED WITH COBALT

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Pure red-cell aplasia is aplasia of the red-cell forming tissue of the bone marrow and leads to chronic refractory anæmia. Unlike what happens in the condition generally termed aplastic anæmia (an unsatisfactory description in view of the hæmatological findings), in pure red-cell aplasia the bone marrow and the peripheral blood show failure of development of the erythroid series alone granulocytopoiesis and the production of platelets being normal

We report the following case because this condition is rare because treatment with cobalt was apparently *successful, and to point out the diagnostic features, for* without careful interpretation of the bone marrow cytology cases will pass unrecognised

## Case-report

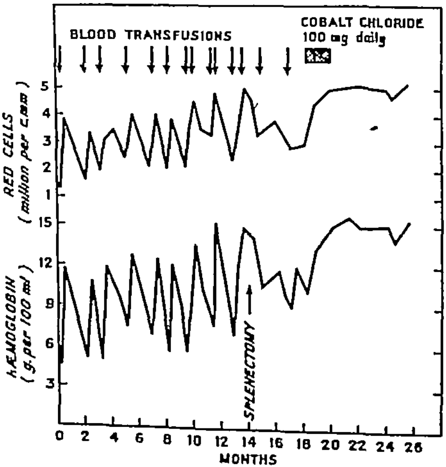
A spinster aged 49 was admitted to Leeds General Infirmary under the care of Dr I Macpherson on Aug 12, 1952 with four weeks history of loss of energy dyspnœa on exertion and increasing pallor

*On examination* she was very obese and severely anæmic with slight sacral œdema and a functional systolic murmur audible at the cardiac apex There was no splenomegaly lymphadenopathy or other positive finding

*Blood examination* showed Hb 4 5 g per 100 ml red cells 1,250 000 per c.mm., reticulocytes 0·1% packed cell volume 12% mean corpuscular volume 96 c µ, mean corpuscular Hb concentration 30% white cells 7600 *per c.mm. (poly* morphs 69%, lymphocytes 29%, monocytes 2%) platelets 350 000 per c mm. and blood group O Rh positive A blood film showed anisocytosis and macrocytosis

*Sternal bone marrow* was cellular with evidence of much depression of erythropoiesis, red-cell precursors representing only 4% of the total marrow cells. All cells of the erythroid series were either pro-erythroblasts or early normoblasts, suggesting arrested maturation. Granulocytopoiesis and the development of platelets were seen to be taking place normally

*Other Investigations* —The urine was normal. A fractional test meal showed histamine-fast achlorhydria. Radiography



Treatment and progress.

of the chest, a barium meal, and a barium enema gave normal results, and examination of the fæces for occult blood was negative The blood cholesterol level was 0 11 g. per 100 ml Electrocardiography showed no abnormality

*Treatment and Progress*—After a transfusion of packed red cells the Hb increased to 11 8 g per 100 ml (see figure) and the patient was discharged on Aug 23, 1952, symptom free and was told to attend as an outpatient In the succeeding six months she was admitted to St James's Hospital, Leeds, four times for blood transfusion

*Investigations*—A urea clearance test showed no impairment of renal function, and intravenous pyelography showed a normal renal tract Further radiography of the chest and alimentary tract and repeated testing of the fæces for occult blood were negative The fæces contained 19 9 g of fat per 100 g of dried fæces (split 70%, unsplit 30%) The serum alkaline phosphatase level was 8 25 units, and radiography of the skeleton showed nothing abnormal. The serum bilirubin level was 0 2 mg per 100 ml The fæces contained 48 5 mg of urobilinogen per 100 g, and the urine 0 4 mg of urobilinogen per 100 ml The indirect Coombs test and Schumm's test were negative Repeated examinations of the blood showed macrocytic normochromic anæmia with almost no evidence of red cell regeneration, judged by the absence of reticulocytes in the peripheral blood and severe diminution of red cell precursors in the bone marrow The bone marrow, however, on all occasions showed that granulocytopoiesis and the formation of platelets were taking place normally, and the leucocytes and platelets in the peripheral blood remained at a normal level

*Treatment and Progress*—Treatment up to March, 1953, had consisted of repeated blood transfusions Oral and intravenous iron and liver extracts had been tried, somewhat empirically because there was no evidence of deficiency of iron or of hæmopoietic principle Neither treatment had any effect on the blood picture From March until August, 1953, various other preparations were prescribed, including vitamin $B_{12}$, folic acid, citrovorum factor, ascorbic acid, and various other vitamins, but all proved ineffective Corticotrophin and cortisone, thyroid extract, and stilbœstrol were also of no value, and during this five month period a further four blood transfusions were required. After careful consideration the patient was advised to undergo splenectomy This seemed justifiable because Loeb (1951) had reported a patient with pure red cell aplasia who had obtained temporary benefit from this operation. She was therefore readmitted to hospital on Sept 4, 1953

*Operation*—After further blood transfusions splenectomy was done on Oct 2 by Mr D B Feather, F.R C S Pathological examination of the spleen revealed no significant abnormality

*Postoperatively* repeated examinations of the bone marrow showed a gradual increase of erythropoiesis Three weeks after operation nucleated red cells accounted for 13 2% of marrow cells, and three months after splenectomy the figure had risen to 22 4% and the bone marrow picture was normal Irrespective of this improvement of the bone marrow cytology the Hb decreased and the red cell count fell after operation, perhaps more slowly, and two more blood transfusions were necessary in the succeeding three months By Feb. 2, 1954, the Hb had decreased to 10 g per 100 ml, and it was decided to try cobalt No drugs had been given since splenectomy four months previously For eight weeks cobalt chloride 50 mg twice daily was given in tablet form There was an immediate sustained response, and treatment was stopped on March 29, when the amount of Hb and the red cell count had become normal For the past seven months the blood picture has remained normal and the patient symptom free, and no further treatment has been required

## Discussion

We have been able to collect only 19 published cases with all the characteristics of pure red cell aplasia severe normocytic normochromic, or macrocytic normochromic anæmia with an absence of reticulocytosis, normal leucocyte and platelet counts, and bone marrow showing aplasia of the erythroid series, granulocytopoiesis and platelet formation being normal Many of these cases have been referred to by Seaman and Koler (1953) and Foy and Kondi (1953), who also reported examples of their own Additional cases have been [illegible] Donnelly (1953), Robson and Sweeney (1948), and Aldridge and Kidd (1953) Other previously published cases resembling pure red cell aplasia have been excluded because of a lack of necessary data, such as bone marrow studies, or because of coexisting leucopenia or thrombocytopenia

The ætiology of pure red cell aplasia is obscure Males seem to be more affected than females, and, whereas 13 of the 19 cases started in adult life, infants were affected in the remaining 6, the anæmia being noticed at birth or shortly afterwards This finding suggests that there may be two forms of pure red cell aplasia congenital and acquired In most cases the cause is unknown, but toxic agents and infection have been suggested Smith (1949) suggested that, in his own case (in a child), the anti A agglutinin elaborated by the mother in pregnancy may have been to blame, although such a mechanism has not been proved by other workers Stronger evidence of a toxic factor is given by Strauss (1943), who described the onset of pure red cell aplasia during sulphonamide therapy, the cessation of treatment led to immediate spontaneous recovery Seaman and Koler (1953) also described a case where sulphonamides may have been a predisposing agent

Treatment in all but 4 cases has proved ineffective Blood-transfusions have produced temporary symptomatic improvement, but the condition has eventually proved fatal One patient recovered spontaneously (Strauss 1943), and Loeb (1951) noticed temporary improvement following splenectomy and treatment with corticotrophin and cortisone Splenectomy, however, although followed by improvement in the bone marrow picture, failed in the present case to increase the Hb and red cells, and corticotrophin and cortisone were both ineffective Foy and Kondi (1953) described a maximal reticulocyte response with complete hæmatological recovery following the administration of riboflavine, and (unknown to us at the time) Seaman and Koler (1953) reported full recovery in a patient after two months' treatment with cobalt chloride

The influence of cobalt on erythropoiesis in animals has been known for several years Waltner and Waltner (1929) showed that an excess of cobalt given to animals produced a polycythæmic state, an observation which has been confirmed by numerous investigators using different species of animals A deficiency of cobalt in certain species leads to anæmia (Filmer 1933, Cartwright 1947) Although there is no evidence that a true deficiency of cobalt occurs in man, these observations on animals and more recently the detection of an atom of cobalt in the molecule of vitamin $B_{12}$ have led to many reports of the effect of cobalt in patients with various refractory anæmias Beneficial effects have been reported in the anæmias associated with chronic infection (Robinson et al 1949), chronic renal disease (Gardner 1953), cancer (Shen and Homburger 1951), sickle-cell anæmia (Wolf and Levy 1954), and Mediterranean anæmia (Muratore 1951)

The satisfactory response to oral cobalt in the present case of pure red cell aplasia supports the observations of Seaman and Koler (1953) Although the follow up in both cases is still too short for us to be certain that a permanent cure has taken place, an early trial of cobalt therapy in the treatment of this rare and generally fatal disorder of erythropoiesis is indicated

## Summary

A case of pure red-cell aplasia in a woman aged 49 is described in which complete hæmatological recovery followed two months' treatment with cobalt chloride

Previous treatment with iron, liver extracts, vitamin $B_{12}$, folic acid, citrovorum factor, œstrogens, thyroid extract, and corticotrophin and cortisone was ineffective, and blood-transfusions were only of temporary benefit

Splenectomy led to an increase in red-cell precursors the bone-marrow but no increase in Hb and red cells

We thank Dr L Macpherson for permission to study and blish this case.

ADDENDUM

Since this paper was submitted J N M Chalmers d K. Boheimer (*Brit med J* 1954, ii 1514) have ported two cases of pure red-cell aplasia associated th thymic tumours. In one temporary hæmatological provement followed thymectomy and both benefited om treatment with corticotrophin In the present case ere was no obvious evidence of a thymic tumour

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# Medical Societies

## ROYAL SOCIETY OF MEDICINE

### Coronary artery Disease

A JOINT meeting of the sections of epidemiology and reventive medicine and of pathology was held on arch 1 under the chairmanship of Prof L P GARROD discuss coronary artery disease

#### MORPHOLOGY

Prof. T CRAWFORD opened the discussion with an count of the morbid anatomical features of coronary therosclerosis emphasising that the effects of plaques the calibre of the lumen was difficult to assess The ual macroscopic examination of the coronary arteries necropsy was inadequate he made three-dimensional diographic studies after injection of a radio-opaque aterial Examples of such radiographs contrasted the ealthy coronary tree with one which was grossly irregular wing to atherosclerosis Slides showed the much thicker tima in normal coronary arteries than in other arteries thers demonstrated early intimal lesions with thickening d a small amount of fat

Such fat might be distributed either in patches or ffusely Later this fatty material became separated from the lumen by a laminated layer of collagen Thrombosis might be followed by retraction and a further crease in the thickness of the intima Alternatively the thrombus might organise and recanalise

Duguid's work showing the part played in the production of atheromatous plaques by repeated deposition of fibrin on the intima was most important Incomplete rganisation of these deposits led to appearances which ere indistinguishable from the classical atheromatous plaque Intimal thrombosis was however only a stage in the development of the fully formed lesion

#### EXPERIMENTAL ATHEROSCLEROSIS

Dr J E. FRENCH noted that atherosclerosis occurred spontaneously only in man It could be produced rimentally in various animals—in rabbits and chicks xcessive cholesterol feeding in dogs by this method bined with impairment of thyroid function and in us monkeys by an excess of dietary cholesterol after a deficient in methionine Rats were particularly resistant to cholesterol feeding Except for some lesions in the rat these experimental lesions consisted essentially of lipoid accumulations They had this in common with the fully developed lesions of atherosclerosis in man and the chemical composition of the lipoid suggested that it originated from plasma lipoids In animals in which atherosclerosis was produced experimentally

1 Hypercholesterolæmia was common to all except in rats where lesions could be produced solely by a dietary deficiency *of choline*

2 The severity of the atherosclerotic lesions was not directly related to absolute concentration of plasma-cholesterol the stability of the plasma-cholesterol as a colloidal solution was more important

It appeared that the distribution of cholesterol between the lipoproteins and the larger β lipoproteins was similar in animals and in man In dogs there was normally a plasma-cholesterol concentration similar to that in man but in dogs 80% was associated with α lipoprotein compared with 20% in man As experimental atheroma developed in the dog an increasing amount of cholesterol became associated with the β lipoprotein fraction Eventually this greatly exceeded the α lipoprotein fraction It had been suggested that the presence of a high concentration of cholesterol containing β lipoprotein in the blood was a significant factor in atherogenesis

Gofman and his collaborators had furthered the theory of the importance of the β lipoproteins in atherogenesis and separated the β lipoprotein complex into parts with different densities (measured in Svedberg units of flotation) A significant degree of correlation had been claimed between lipoprotein components of $S_f$ 10–30 and the development of experimental atheroma in animals The $S_f$ 10–30 lipoproteins had also been identified in the blood of cebus monkeys with atheroma.

The $S_f$ 10–30 lipoproteins, although macromolecules did not appear to be responsible for the visible lipæmia in cholesterol fed rabbits. Much of this was due to visible lipoid particles which could be separated by centrifugation at relatively low speeds Chylomicra occurring in the blood of normal animals after ingestion of lipoid, appeared to be broken down to a more diffusible form by a similar process to that in heparin clearing But the visible lipoid particles in the blood of cholesterol fed rabbits seemed to be removed from the blood only by phagocytosis

The method by which abnormal lipoid crossed the endothelial lining to be deposited in the intima was widely considered to be one of filtration Acceptance of this hypothesis was implicit in Gofman's theory of atherogenesis An alternative was that foam-cells adhere to the aortic endothelium and are either overgrown by it or else migrate inwards It had been suggested that unstable plasma lipoid material might behave similarly Experiments could help to determine whether atheroma began under or over the endothelium

#### DIET IN PATHOGENESIS

Prof H W FULLERTON considered briefly the evidence that there was an association between atheroma and a high dietary intake of fat He accepted the contention of Duguid that fibrin deposits formed the essential starting point of atheroma

The dietary intake of fat had been increasing for many years in this country along with growth in incomes and so had the incidence of coronary thrombosis usually regarded as secondary to atheroma Two further points linked the intake of dietary fat with the incidence of coronary thrombosis Keys had shown that the mortality from degenerative heart disease was higher in countries whose inhabitants had high intakes of dietary fat than in others and mortality from cardiovascular diseases appeared to decrease in Norway during the 1939–45 war

He had found experimentally that reduced clotting time was associated with the lipæmia which followed a meal rich in fat, and that this increased blood coagulability was present only when the intake of fat was high He therefore suggested that one factor responsible for the intermittent deposition of fibrin on the arterial intima was the ingestion of meals rich in fat There was probably considerable individual variation in this mechanism, and also possibly a sex difference The lipæmia following fat ingestion was certainly greater in elderly subjects and in those with coronary-artery disease Fibrinolysis might also be important in coronary thrombosis The question of coronary thrombosis must be considered in the light of any theory of the pathogenesis of atheroma

### EPIDEMIOLOGY OF CORONARY ATHEROMA

Dr J N Morris considered the problem in its public health setting Secular trends in mortality-rates showed a slowing in the fall of the male death rate in middle age during the past thirty years, this slowing was not evident in the female death rate Duodenal ulceration, ischæmic heart disease, and bronchial carcinoma affecting males especially, and common in middle age, were mainly responsible for these trends Ischæmic heart disease was the biggest single factor Social class I, the inhabitants of large towns, and physically inactive workers—bus drivers as opposed to conductors—had the worst records for this disease Farmers and agricultural workers were particularly free of it

Epidemiologically, a pathological study of coronary atherosclerosis was needed Dr Morris had appealed to pathologists throughout the country for data, and there had been a very generous response Analyses of pooled hospital necropsy records, now being made and adjusted to give an idea of what was happening in the population as a whole, showed that the proportion of men with much coronary atherosclerosis steadily increased to as high as 20–25% by the age of 70 years, and the proportion with stenosis in a main coronary artery to 30–35% Those dying of hypertension had substantially more coronary atherosclerosis than the rest of the population In a fifth of the deaths from ischæmic heart disease nothing particular in the way of coronary atherosclerosis was found, but the majority did have a considerable amount Dr Morris emphasised that although many were susceptible to ischæmic heart disease by virtue of the condition of their coronary arteries, it developed in only a minority of these There was no 1 1 relation between coronary atherosclerosis and ischæmic heart disease, no increase of coronary atherosclerosis alone in the population had been found, for instance, in recent years He considered the factors that were needed for the conversion of the pathological entity, coronary atherosclerosis, into clinical ischæmic heart disease, and the need to identify causes in the environment that were related to this conversion

### DISCUSSION

In the discussion that followed, Dr Z A Leitner was gratified that Professor Fullerton supported his postulate about the importance of increased dietary fat intake in atherogenesis [1 2] He presented further evidence that many of the known causes in the development of atherosclerosis including such hypothetical ones as physical and emotional stress, raised the blood lipid levels He drew attention to the biochemical differences in the proportion of the α and β lipoprotein fractions between males and females—a difference which apparently could be influenced by hormone administration The very pronounced and characteristic increase of the β lipoprotein fraction in males seemed to be related to the greater incidence of coronary accidents in males, and clinical trials on a considerable scale were proceeding in several centres to correlate the therapeutic decrease of the β lipoprotein levels in males suffering from coronary disease with their subsequent clinical condition

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[1] *Lancet* 1951 I 1078

[2] *Med World Lond* 1954 81 249

## MANCHESTER MEDICAL SOCIETY AND LIVERPOOL MEDICAL INSTITUTION

A joint meeting was held in Manchester on March 2, under the chairmanship of Dr H P Fay, president of the Manchester Medical Society

### Virus of Varicella and Zoster

Prof A W Downie said that association of chickenpox with zoster is well recognised, in that child contacts of zoster cases not infrequently develop a clinical infection indistinguishable from chickenpox Yet, because of the difference in clinical picture and pathology, and the difference in age and seasonal incidence, there has been some hesitation in accepting the thesis that zoster is an infection with varicella virus Three different views seem to be held (1) that one virus causes the two conditions, (2) that the two clinical entities are due to different but closely related viruses, and (3) *that some cases of zoster, but only some, are caused by varicella virus* The recent investigations of Hope Simpson [1] in one of the Shetland Isles seem to show conclusively that the chickenpox derived from zoster cases is in no way different from ordinary chickenpox The clinical picture, interval between serial cases, and infectiousness are the same, and an attack of the one kind of chickenpox confers immunity to the other The experimental infections of children with zoster vesicle fluid by Kundratitz and by Bruusgaard show that such infections sometimes result in clinically typical chickenpox which leaves an immunity to further inoculation with vesicle fluid from zoster or chickenpox cases

Laboratory investigations have been hampered by lack of susceptible laboratory animals, but such information as is available reveals no differences between the virus from chickenpox and zoster patients The histological features of the skin lesions are the same, by electron microscopy the virus particles are identical and are agglutinated by convalescent serum from either type of case Antigen in vesicle fluids cross reacts completely in complement fixation tests with convalescent sera Recently Weller has infected tissue cultures of human tissue with virus from vesicle fluid of zoster and chickenpox patients Both materials produce the same kind of cytopathogenic effects with the appearance of multinucleated cells and typical intranuclear inclusions in the cells of the lesion By an ingenious indirect technique using fluorescent antibody he has shown that infected cells in tissue culture bind antibody in convalescent sera from either zoster or chickenpox cases

The laboratory findings therefore support the view, based on clinical and epidemiological observations that zoster is a particular kind of infection with varicella virus The facts that zoster usually occurs at an older age than varicella, that the majority of zoster patients have previously had varicella years previously, and that zoster commonly arises in persons having no known contact with varicella or zoster cases and may be precipitated by X irradiation, trauma of injection, &c suggest that zoster in many instances is due to activation of a latent virus in persons whose general immunity may have waned

### Some Methods of Investigating Inherited Factors in Disease

Dr C A Clarke first discussed the ABO blood groups as a polymorphic system and explained that, because the percentage in the population remained constant, equal ns must be maintained by a balance of advantages disadvantages. He recalled the work of Aird and olleagues who in 1953 had shown that there was an ciation between carcinoma of the stomach and blood p A In the following year the same workers had d that peptic ulcer was associated with a marked s of group O

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[1] Hope Simpson R E *Lancet* 1954, ii 1299

r Clarke gave the results of a similar investigation verpool. From three hospitals 1407 cases of ulcer been analysed and it had been found that whereas distribution of the blood groups in gastric ulcer was al, in duodenal ulcer there was a distinct swing to om A 59 6% of the cases were O and only 20% A corresponding control figures being 49 1% O and % A

he control series had been obtained from two sources the over-all blood group distribution of the three hospitals uding ulcers, in 1948–54 ; and (2) blood-donors obtained a the Nuffield Blood Group Centre As no significant rence had been found between these two sets of controls t from the hospitals had been used because it was much ger (15,277 cases)

r Clarke considered whether the association between od group O and duodenal ulcer might be due to egenation rather than to causal relation An lysis of duodenal ulcer within families was helping to re this problem The number of sibships so far estigated was only 53 this was not nearly enough llow of any definite conclusion but the current data give a hint that the association was present within families

ecause of the reciprocal relation between group O group A in respect of duodenal ulcer and cancer of stomach it was worth investigating other diseases hich the secretion of hydrochloric acid was abnormal chanan and Higley [2] had shown that in 457 cases of nicious anæmia there was a higher incidence of group A the expense of O than in the general population Clarke thought that this finding supported his idea the ABO locus might contain one genetic factor onsible for the amount of hydrochloric acid secreted n the direction of hyperchlorhydria and A in the ction of hypochlorhydria

urning next to diabetes mellitus, in which duodenal r is rare and achlorhydria rather common Dr Clarke ribed an analysis by R B McConnell on the d group distribution of 815 diabetics from the etic clinic at the David Lewis Northern Hospital rpool [3] This showed that in the under 30 age group cases) mainly consisting of patients (predominantly ) who were non obese and who required insulin re was a swing of 12% from group O to group A pared with the controls ($\chi^2 = 8\ 21$) In the older group usually associated with obesity and insulin sitivity the blood group distribution was normal believed that the finding in the younger age group ht support his hypothesis and the next step was to d out the age incidence and blood group distribution chlorhydria in diabetics

r Clarke showed how the ABO blood groups were of as marker genes He described a linkage between ABO locus and hereditary onycho-osteo dystrophy patella syndrome) recently discovered by Renwick Lawler [4] at the Galton Laboratory

n the third part of the paper he described how cular biopsies obtained from fertility clinics provided ent material for human chromosome studies The had come from Mr J H Burnett D PHIL. of the artment of botany and emphasised the value of eration between university departments

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# Reviews of Books

## Artificial Respiration

With Special Emphasis on the Holger Nielsen Method
T O GARLAND M.A M D D P H London Faber & Faber 1955 Pp 60 6s 6d

THIS short book will be useful to all concerned in teaching and practising resuscitation It is practical giving enough theory only to make it clear why some manœuvres produce better results than others.

The emphasis is mainly on the now officially recommended Holger Nielsen method and secondarily on the Silvester and Eve rocking methods Other and older manœuvres are briefly described An interesting account is given of the observations originally made by Pask in Oxford—courageous observations, all too rarely mentioned which were the forerunners of the intensive and important work done later in the U S A A few tables show clearly the large ventilation induced by the Holger Nielsen method as compared with others, particularly the Schäfer method. The photographs are clear and one subtly emphasises that the Holger Nielsen method does not need muscular strength by showing a young girl applying it to a man

The author points out that efficient first aiders should know more methods than one since no one method is suited to all circumstances. He describes how artificial respiration may be applied with the patient in a sitting position where it is not possible for him to be laid down as in a small boat or in pole top rescue after electrocution when speed of treatment is even more desirable than usual He also describes how the rocking method may be applied for short periods and immediately in rescue to both children and adults He recommends (what is now agreed) that oxygen rather than a mixture of oxygen and carbon dioxide should be used for resuscitation.

The book takes very little time to read and deserves the attention of doctors, some of whom know less than laymen about resuscitation methods

## Radio-isotope Conference 1954

Vol I Editor: J E JOHNSTON 1954 Pp 418 63s

## Radiobiology Symposium 1954

Editors: Z M BACQ and PETER ALEXANDER 1955
Pp 362 60s
London Butterworth Scientific Publications.

THE fashion of the scientific 1950s of printing the proceedings of international conferences is valuable only if publication is rapid In both these instances the publishers and the editors are to be congratulated on issuing reports within six months

The work recorded at the radio isotope conference held at Oxford last July was in no sense revolutionary In the sessions on therapy diagnosis, animal physiology and pathology biochemistry and plant nutrition there is nothing that will rank in history as outstanding but there is much sound effort As might be expected radioactive isotopes still have their most useful rôle in physiological experiments on animals or in the glassware of the biochemist—now often vastly more complex than the test tube Thus the three sessions each on physiology and biochemistry are much better value than the two clinical sections ; but the clinician may dip into them with advantage : for on the physiology of today as illustrated here next year's diagnostic tests may be founded

At the radiobiology symposium held at Liège last August physical chemists described the effects of radiation on model chemical agents such as lipids An oxidising effect is usually predominant and the peroxides found in vivo in mice are sought Desoxyribose nucleic acid (D.N.A ) is also of course a substance for study and so less obviously to the biologist is polymethylmethacrylate Oxidation is of interest not only to the chemist Bacteria bacteriophage and mice are the subjects for experimentation with anoxia and oxygen accepting substances. Some of these last mentioned like cysteamine are being widely used in investigation since they give measurable prophylaxis against radiation. Spleen and bone marrow injections on the other hand are equally in the news since they are effective as therapy in reducing mortality Reversely radiosensitisers are of value in clinical radiotherapy Taking the cell to bits after it has been irradiated of approach The biochemists look at such processes as phosphorylation of mitochondria and D N A synthesis the cytologists look at disordered chromosomes

### Color Atlas of Pathology

Vol II Prepared under auspices of the U S Naval *Medical School, National Medical Center, Bethesda* Philadelphia and London J B Lippincott 1954 Pp 450 £7

THIS admirable and well-produced book will be read with profit not only by students and postgraduates but also by pathologists in need of an interesting refresher course

The subjects covered include the endocrine glands, the reproductive organs, the breast, and skin The illustrations, some of which are clinical, are nearly all excellent, and they are all helpful and carefully selected Each section is introduced by a few pages of text, then follows the photographs, three to a page with full and lucid captions outlining the case histories and the pathological findings

Rear-Admiral Lamont Pugh, the surgeon-general, in his foreword pays a well-earned tribute to the team of authors, photographers, and lithographers who have contributed to the work Inevitably, in a book of this kind, the price is too high for most of us, for this reason it is to be hoped that it will be included in medical-school libraries

### Porphyrins

*Their Biological and Chemical Importance* A VANNOTTI, University professor and director of the University Medical Polyclinic, Lausanne Translated by C RIMINGTON, D SC, F.R S, professor of chemical pathology, University of London London Hilger & Watts 1954 Pp 258 50*s*

THE original German edition of Professor Vannotti's monograph, *Porphyrine und Porphyrinkrankheiten*, was rightly regarded as a classic, hence the new English edition, translated and revised by Professor Rimington, and containing new material, is especially welcome It is a pity, however, that, at a time when there have been major advances in this field, there has been so long a delay between preparation of the manuscript and publication Thus there is but a scanty account of the incorporation of labelled glycine and acetate into porphyrins and related compounds, there is no mention at all of the brilliant work of Shemin in elucidating the source of each carbon atom in the porphyrin structure, and only a footnote refers to the identification of porphobilinogen, the colourless precursor of porphyrin, excreted in acute porphyria At no point is it made clear that, according to modern views of porphyrin biosynthesis, protoporphyrin is formed (even though via an indirect pathway) by decarboxylation and dehydrogenation of uroporphyrin On the contrary, some emphasis is made regarding the demonstration by van den Bergh that protoporphyrin was converted to coproporphyrin by perfusion through the liver—an observation which has not been confirmed and upon which doubt has been cast The very recent work on δ-amino-lævulinic acid could perhaps scarcely have been included

The chapter on physicochemical aspects of porphyrins has a number of valuable tables presenting the wavelengths and extinction coefficients of the absorption bands of the various porphyrins and—even more useful—their fluorescence spectra The short chapter on methods of extraction and qualitative and quantitative determination of porphyrins is little more than a catalogue of the various methods proposed, and does not discuss them critically A brief but useful account of porphyrins in Nature, in which previous work on the porphyrins of bacteria and of yeast is particularly well reviewed, is followed by two chapters dealing with the physiology and pathology of porphyrins in man Professor Vannotti discusses, from his wide clinical experience, numerous conditions in which porphyrin excretion is increased or abnormal, and presents some interesting data on the time relations between porphyrin excretion and such pathological disturbances as hæmorrhage, anæmia, and cardiac insufficiency One of the best sections deals with the evidence [illegible] d poisoning there is an inhibition of the utilisation of iron in the synthesis of hæmoglobin in the erythroblast, and consequent elimination of type-III porphyrins A 56-page chapter on porphyria is one of the best accounts of the clinical aspects in English It is a pity that the author does not emphasise more the great diagnostic importance attached to the finding of porphobilinogen in the urine A final chapter, on treatment, probably gives too much weight to the relations between vitamins and the porphyrias Treatment of this disease is still symptomatic and palliative, and spontaneous remissions have too often been attributed without foundation to some specific treatment

In spite of the lamentable delay in publication and the consequent absence of the recent advances in this field, this book is a valuable contribution to the literature of porphyrins and porphyria and can usefully be read by clinicians likely to encounter the condition as well as by laboratory workers attempting to elucidate the function of these pigments and the mechanism of the porphyrias

### Rheumatic Fever

*"Disease a Month" Series, no 1* LOWELL A RANTZ, associate professor of medicine, Stanford University School of Medicine Chicago Year Book Publishers London Interscience Publishers 1955 Pp 35 Twelve monthly issues, 65*s*

THE publishers of this new series are convinced that "the busy physician unable to maintain a routine schedule of comprehensive reading will eagerly find time to read regularly a single and original 30 to 40 page monthly presentation of high authority" The first issue by Dr Rantz, of Stanford University Medical School, an authoritative, balanced, and practical summary of modern views on the pathology, prophylaxis, and management of rheumatic fever which fully justifies the publishers' description It is possible to feel a niggling doubt about this sort of thing There is no real substitute for the eclectic approach, however laborious If the sifting is done for us, can we distinguish fact from opinion and experience from prejudice? Nevertheless this series will be welcomed as useful and convenient summaries It is, after all, intended as no more

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**Psychometric Methods** (2nd ed New York and London McGraw Hill 1954 Pp 597 61*s*)—Prof J P Guildford recognises that the problems of psychometrics are not so much problems of pure mathematics as practical problems of collecting, comparing, classifying, and inter-correlating psychological data From a concise account of the value of measurement itself, and the mathematical concepts involved, he proceeds to discuss methods of conducting the simplest to the most advanced statistical operations required to determine the central trend, dispersion, correlation, and factor content of different kinds of psychological measurements Quite justifiably he gives precedence to his own and largely orthodox procedures, but he describes the contributions of other workers in this field in a way which brings the subject into historical perspective and makes the book enjoyable Copious references are given at the end of each chapter and are clearly indexed at the end of the book Even in 600 pages he has had to limit his discussion of this subject, which is at present almost a major psychological industry To make room for the enormous amount of new material it has been necessary to eliminate most of the statistical treatment given in his first edition, and to refer readers to his *Fundamental Statistics in Psychology and Education* In psychometrics we are notoriously apt to destroy the qualities of human behaviour which will not submit to measurement, or from their very originality cannot be classified and counted, but Guildford conveys a vitality behind his techniques and a generous outlook which renders his exposition free from either defensive dogmatism or aggressive objectivity

**La rate et ses maladies** (Paris Masson 1954 Pp. Fr 2200)—This monograph is a fair summary of present-day ideas on diseases of the spleen, but contains little that is not already well known to anyone who follows the literature. The only unusual sections—on splenomegaly due to parasitic diseases and on splenomegaly due to tuberculosis—reflect Dr Gabriel Gelin's special experience in North Africa

# THE LANCET

*LONDON SATURDAY MARCH 12 1955*

## The Accident Syndrome

THE notion that some people are particularly sus-ptible to accidents is nowadays generally accepted d some authorities have gone so far as to say at 85% of accidents are contributed by 15% the population But who exactly are the accident one ? Do they really form a convenient homogeneous oup about whom it is possible to make statements d predictions ? Students of the subject are inclined agree that they do, but they agree about very tle else Nothing could be less similar than the rtraits drawn by different observers of this ham nded and elusive section of the community

Those described by FLANDERS DUNBAR[1] in 1942, re quick minded impulsive people, given to imme ate action inarticulate about their feelings, apt to vorce and remarry easily, unusually healthy, seldom f work, not subject to colds or indigestion consciously unconsciously hostile to authority but rather reful to avoid conflict with it

> They came, typically from families in which both rents were strict but they had usually left home early been orphaned and had thus lived with their parents r a shorter time than most children Their education d often been interrupted, usually because they had iled to finish any training course they undertook and eir work history was of many and diverse jobs Usually st before the accident there had been some conflict ith authority, parent, or spouse, from which escape had emed impossible

NBAR made these observations on a group of acture patients in hospital whom she was studying r comparison with patients suffering from coronary clusion. It came to her as a surprise that 80% of e patients in this fracture ward had had two or ore accidents She found the accident habit to be pecially common among those aged 15–25

A rather different picture comes from J W HITFIELD[2] who recently made a study of accident one miners

> He found they fell into two groups according to age The younger men were heavy, muscular and well ordinated but not very quick at spotting when danger reatened The older men were quick enough to see e danger but not quick enough at getting out of the ay The young ones as he put it, failed in appreciation e older ones in performance and neither the slow tted young nor the slow moving old quite fits in with e casual impulsive people described by DUNBAR

n the Milroy lectures which he gave at the Royal llege of Physicians on Feb 8 and 10 J A SMILEY rew yet another picture—of workers in an aircraft ctory, given not only to accidents but ailments Compared with controls these workers lost thrice as much time from work and attended the medical department thrice as often for causes other than accidents They were also far more liable to peptic ulceration than their fellows, and more often away from work with conditions diagnosed vaguely by their doctors as fatigue, neurasthenia, gastritis rheumatism and the like (Nowadays DUNBAR[3] too, emphasises a relation between accident-proneness and minor ailments ) Some 72% of them, as against 8% of controls, were emotionally unstable, or passing through periods of emotional crisis or strain at the time of the study Young married men aged 26–35 with children were often sharing quarters (because of the housing shortage) either with their own or their wives parents Many members of the group as a whole showed palmar, plantar and axillary sweating, and in moments of stress, they were either unable to micturate or developed frequency, some also showed mild transient albuminuria Many of these symptoms in SMILEY's view, suggest a loss of balance between the sympathetic and parasympathetic systems, influenced by abnormal emotional activity and mediated by the hypothalamic region of the brain Lesions in this region (as we remarked last week[4]) have also been shown to be associated with peptic ulceration.

Why should these three observers see the accident-prone so differently ? Perhaps because they attached rather different meanings to the term "accident" DUNBAR's original group had fractured themselves badly enough to get into hospital WHITFIELD counted only those accidents which had kept his miners away from work for three days or more SMILEY, on the other hand, included all accidents reported to the medical department, and he had good reason to believe that, during the period under review, extremely few accidents whether major or minor, were not reported Are there perhaps different kinds of accident-prone prone to different kinds of accident —some impulsively shattering their bones, some moodily pinching their fingers in machinery, and some pursuing dangerous callings for which slowness of wit or limb unfits them ? Does the choice of accident, in fact depend partly on temperament ? Certainly, the greater the variety of accidents taken into account the less precise the portrait of the accident-prone appears MORRIS S SCHULZINGER[5] has studied the case-histories of all the accident patients he encountered between 1930 (when he entered the industrial and general practice of medicine) and 1948 they amount to 35,000 cases, of which 27,000 were industrial and 8000 non industrial He divides those who had had more than one accident into "normally adjusted" (group A) and "irresponsible and maladjusted" (group B), and finds that though in both groups, accidents were "essentially an affliction of youth," yet there was a higher incidence of repeated accidents in group B than in group A Males had a higher incidence of accidents than females He finds no reason to suppose that 85% of accidents befall 15% of the population on the contrary, three quarters of all these accidents were the solitary experiences of large numbers of individuals He notes as others have done a definite seasonal pattern numbers of accidents increasing from a low figure in February to a peak in June then declining, and a similar daily pattern rising from a low figure at 5 A M to a peak at 5 P M and then falling

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[1] [illegible] 1943 1 879 ; see also *Lancet* 1954 ii 1285

[2] *Brit J industr Med* 1954 11 126 see also *Lancet* 1954 i 133

[3] *Emotions and Bodily Changes* p 63 4th ed Columbia University Press 1954 [illegible]

[4] *Lancet*, March 5 1955 p 10[illegible]

[5] *Arch industr Hlth* [illegible] 11 88

Six types of incident accounted for 80% of non-industrial accidents "falls, aggressive behaviour, handling objects, foreign bodies, motor vehicles, and stumbling into objects" The superstition that one accident is likely to be the first of a series of three seems to gain prestige from the fact that "accidents often occur in chain fashion, as if one accident acted as a trigger mechanism for another accident, or series of accidents, in the individual or the group" Moreover there seem to be some who have a predilection for certain types of accident or for injury to certain parts of the body SCHULZINGER, too, finds that the probability of accidents is increased by emotional stress or strain Indeed, from his findings and those of others he deduces that one can predict with reasonable certainty when and to whom an accident is most likely to happen

> Let the young man of 21 beware of a hot and humid summer day in June or July, at a weekend, or while he is on holiday, especially if he is an aggressive type, or is driving a car, and more particularly if it is late afternoon or early evening Such young men are the most likely people to have accidents, especially if they are inexperienced drivers, or have taken alcohol, or are driving too fast, or are tired, or have psychological conflicts, or are suffering from anxiety, hostility, frustration, or guilt, and few young men of 21 manage to avoid all such weaknesses If they are irresponsible and maladjusted, and grew up in a home subject to violence and strife, under the care of over-authoritative parents or parent-substitutes, their chances of an accident are much increased How much more hopeful (for the time being) is the outlook for a healthy well-adjusted girl of 13, born and reared in a normal, secure, and loving home in which both parents are well adjusted she is the least likely person, he found, to have an accident

SCHULZINGER concludes that we should discard the idea of accident-proneness and accept instead a concept of accidents as a disease syndrome, for which preventive measures are possible The accident prone are, in his view, not a fixed group but a shifting one, with new people constantly leaving or joining The excessive liability to accidents of the young usually disappears with age, and those who suffer repeated accidents tend to improve "with learning, with physiological and psychological adaptation, with the development of more adequate psychological defences, with the elimination of hazardous exposure " Accidents, then, should be looked on as a clinical entity, he thinks, rather than a problem in safety, and doctors should take responsibility for diagnosing and treating the physical, mental, and emotional disorders which play a part in accidents

Nevertheless inside this wide concept there may be room for the smaller notion of accident proneness Surely it is useful to look, as WHITFIELD and SMILEY have done, for those in a circumscribed industrial group who have the accident habit, and to discover what preoccupations or discontents they are thus avenging on themselves, or what physical or mental peculiarities are hindering them in their calling Some, at least, of these factors may be modifiable, and even an opportunity to unload his griefs may appreciably change a man's attitude By relieving us of the notion that accident-proneness is a life-pattern SCHULZINGER brings this tiresome disability into the itable disorders

## Pharmacology of Reserpine

IT is not yet clear what place reserpine, the active alkaloid of *Rauwolfia serpentina*, will take in the treatment of hypertension Many reports[1–8] have claimed that reserpine represents an important advance, whereas others[9–13] have been more cautious

In laboratory animals and in man reserpine lowers the blood-pressure, slows the heart-rate, increases the intestinal movements, constricts the pupil, and exerts a characteristic sedative action on the central nervous system Even after intravenous administration of the drug, there is an interval of an hour or more before the onset of these effects, which are long lasting The classical techniques of the experimental pharmacologist show that in therapeutic amounts reserpine lacks significant peripheral action Thus it does not inhibit the effects of adrenaline,[14–21] noradrenaline,[14 18 22] acetylcholine,[14 21–23] or histamine[18 21 22] it does not block transmission in autonomic ganglia[14 19], and it does not increase the movements of the isolated intestine[14 17] Nor does reserpine influence the rate, stroke volume, or coronary flow of the isolated heart[10 18 20] or relax perfused blood vessels[14 18 22 24] Finally, instilling reserpine directly into the conjunctival sac does not affect the pupil But many of these effects, which are absent after administration of amounts equivalent to therapeutic doses, are found after administration of large doses The effects of reserpine observed clinically are, it seems, due to actions within the central nervous system The fall of blood-pressure in animals is due to lowering of the peripheral resistance by vasodilatation, cardiac output does not fall significantly[20] The central site of this hypotensive action is confirmed by the observation that reserpine abolishes pressor reflexes, the pathways of which traverse the central nervous system These reflexes include the pressor responses to stimulation of the sciatic nerve,[14] compression of the carotid sinus,[14 20 21] or stimulation of the central end of the cut vagus[14 20 21] On the other hand, reserpine does not influence the pressure rise induced by stimulation of the efferent vagus[14 20 21]—a response that does not

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1 Vakil P J *Brit Heart J* 1949 11, 350
2 Wilkins R. W Judson W E *New Engl J Med.* 1953 248, 1
3 Löffler W, Essellier, A F, Prött, F, Wegmann, A *Schw-med Wschr* 1953, 83 1012
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8 Livesay W R Moyer, J H Miller, S I *J Amer med A* 1954 155, 1027
9 Freis, E D Ari R *Ann N Y Acad Sci* 1954, 59 45
10 Moyer J H *Ibid*, p 82
11 Douthwaite A H *Lancet*, 1954, i 1345
12 Doyle A E Smirk, F H *Practitioner* 1955, 174 135
13 See *Lancet* 1954 ii, 741
14 Bein H J *Experientia* 1953 9 107
15 Trapold J H, Osborne, M. Yonkman F F *Fed Proc* 195 12, 373
16 Bein H J Gross, F, Tripod, J, Meier, R. *Schweiz med. Wschr* 1953 83, 336
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21 Gourzis J T Sonnenschein, R R. Barden, R. *Proc Soc Exp Biol N Y* 1954, 85, 463
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23 Barrett W E Rutledge, R A, Rogie B *Fed Proc* 1954 13 334
24 Mueller, J M., Schlittler E, Bein, H J *Experientia* 195 8, 338
25 Ray G K Roy P K Dasgupta S R, Werner G *Arch exp Path Pharmak* 1953, 219 310
26 Tripod J Bein H J Meier, R *Arch int Pharmacody* 1954 96, 406

epend on the integrity of the central nervous ystem—and it does not affect the secretion of pressor mines by the adrenal cortex.[14] There is no evidence hat reserpine affects humoral pressor agents

The miotic action of reserpine [14–17 19 20 25 27] provides profitable field of study This effect is not very reat in man,[3 9] but in the dog and other animals it is he sign which, after administration of the drug ppears first and persists longest After intravenous njection of reserpine the pupil of the dog begins to arrow in half an hour, in two hours it is half the nitial size and it returns to normal only after more han six hours, the light reflex of the pupil is not minished [14 8] If the eye is denervated by excision f the ciliary ganglion reserpine has no miotic effect hich confirms that the drug does not act at the eriphery [25] The miosis might, then, be due to central imulation of the parasympathetic system or to entral inhibition of the sympathetic system The ictitating membrane of the dog and cat has no rasympathetic innervation and contraction and laxation of this membrane are due to sympathetic imulation and inhibition respectively Reserpine auses relaxation of the nictitating membrane,[14 16 25 27] nd this has been taken to support the view that erpine acts by central inhibition of sympathetic one Several of the other effects of reserpine might be plained similarly—for example, the increased intes inal motility, the slowing of the heart and perhaps en the fall in blood pressure HESS [28] found that imulation of certain areas of the mesencephalon sulted in hypotension bradycardia, diarrhœa and iosis The similarity of this syndrome to the effects reserpine was pointed out by BEIN et al [16] who ondered whether reserpine might act through these rticular areas Clinical observation gives some pport to this suggestion In a few hypertensive tients treatment with reserpine has aggravated isting bronchial asthma, renal colic biliary colic, ulcerative colitis [4 12] and such effects might be ue to relative parasympathetic dominance In man is not clear what part sympathetic tone plays in aintaining the blood pressure The hypertensive esponse to cold and to posture both thought to be ediated through the sympathetic system are little fluenced by reserpine [17 19 29] Moreover miosis is often found in man, and it is apparently unrelated ll in blood pressure

nother unexplained property of reserpine is the rval before the onset of its action, even after avenous administration It is very insoluble, and bably the delay represents simply the time required an adequate concentration to reach the recep- [14 29] the smaller the dose the longer is the nt period [14] The characteristic latency is evident the organ bath,[16] where the action of reserpine ists and is even enhanced after the fluid containing drug has been washed out [30] These findings nforce the view that the drug has an intracellular of action [20] A less likely explanation of the drug s ency is that it represents the time required for a tabolic transformation [20 31]

The central sedative action of reserpine is not the cause of its effect in lowering blood pressure But this central action is a useful adjunct, in fact, reserpine is now being increasingly used in the treat ment of mental disease [32 33] On the other hand, it can cause mental complications, notably depression in hypertensive patients [12 34] Otherwise there have been no reports of serious toxic actions from protracted administration Whatever its ultimate place in the treatment of hypertension reserpine will stimulate much inquiry into the mechanisms of this disorder

## Hazards in Treating Diabetic Ketosis

IN the main centres the treatment of diabetic ketosis has improved greatly in the past ten to fifteen years owing largely to a round the-clock biochemistry service by which the patient's progress can be accurately followed It is in other hospitals where constant biochemical control is not attainable, that most of the preventable deaths now take place. But avoidance of some of the hazards depends wholly on the clinician's skill Commonly the patient s stomach is distended with fluid, and if this distension is not soon relieved stomach contents may be aspirated, perhaps just as consciousness is returning Similarly it is unwise to rely on oral administration of fluid until the phase of ileus has clearly passed Then again, diabetic ketosis is commonly associated with severe infection such as pneumonia or carbuncle and unless this is promptly treated the patient will remain refractory to the action of insulin

If ketosis has come on gradually there is especial likelihood of severe depletion of fluid with circulatory collapse and renal failure. This should be treated as early as possible by intravenous administration of a fluid designed to replace the extracellular fluid loss, such as the saline-lactate solution recommended by NABARRO and his colleagues [35] BUTLER and others [36] have shown that "physiological' saline solution is in this context distinctly unphysiological The deficit of sodium exceeds that of chloride, and if these are given in equivalent proportions the acidosis tends to increase by virtue of the excess chloride ions It is therefore desirable to give these ions more nearly in the proportions in which they are found in extra cellular fluid—namely 1 3 Na 1 Cl, the anion deficiency being made up with lactate which is metabolised Another possible effect of infusing 'physiologi cal saline to counter the dehydration is hyper natræmia [37] The real need for sodium to correct the acidosis is less than the apparent need for the acidosis is caused mainly by accumulation of keto acids which are metabolised more rapidly than they are formed under the influence of insulin, with release of sodium to balance its normal anions in the blood If the patient's blood pressure fails to rise satisfactorily as a result of infusing saline lactate solution, other measures should be adopted otherwise the patient may die in shock with renal failure Administration of

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[32] Kline N S Ibid, p 107

[33] Noce R. H, Williams D B Rapaport W J Amer med Ass 1954 156, 821

[34] Freis E. D New Engl. J Med. 1954 251 1006

[35] Nabarro J D N Spencer A G Stowers J M Lancet, 1952 i 983

[36] Butler A. M. Talbot N B Burnett C H Stu [illegible] MacLachlan E A Trans Ass Amer Physns

[37] Nichols G Jun Nichols N J clin Invest

hypertonic plasma has the advantages of not involving the delay of cross matching blood, and of returning to the vascular system fluid which may have escaped into the interstitial spaces If hypotension persists, intravenous noradrenaline is a rational remedy

The cornerstone of the successful treatment of diabetic ketosis is prompt administration of sufficient insulin But in the past decade this has perhaps been emphasised rather unwarily, with the result that insufficient regard has been paid to the risk of the patient slipping quietly from diabetic coma into hypoglycæmic coma, and this hazard is especially great where serial blood-sugar estimations are not done MICKS[38] states that he has never heard of fatal hypoglycæmia after overdosage of insulin in diabetic ketosis, but such accidents undoubtedly happen, as is shown by the following case which has been brought to our notice

The patient received insulin 150 units initially, 100 units an hour later, and then 50 units hourly The insulin requirement was assessed by the clinical condition and by urine tests Lack of clinical improvement suggested that she was peculiarly refractory to insulin, but ten hours after treatment was started the urine became sugar-free, and the patient died shortly afterwards without recovering consciousness Blood-sugar levels were not estimated concurrently, but specimens were taken every two hours for estimation next day It was then found that the level had fallen from an initial 801 mg per 100 ml to 237 mg per 100 ml in the first four hours, and had reached 65 mg per 100 ml before death

Several lessons may be learnt from this case first, the unreliability of purely clinical judgment of insulin dosage, secondly, the desirability of parallel measurement of the blood-sugar, which can indicate a safe dosage of insulin, and thirdly, the need for some simple laboratory estimate of the severity of the condition, if the blood-sugar level cannot be estimated at once This need is largely met by a simple, roughly quantitative, test for plasma-ketones with a modified Rothera's powder[39] In diabetic coma insulin resistance is very closely associated with the degree of ketosis[40], so, when the plasma-ketones are found to be disappearing, this is an indication to reduce the insulin dosage and to watch carefully for hypoglycæmia At this stage, too, the intravenous infusion should contain glucose

After the initial phase of intravenous therapy, designed mainly to replace lost extracellular fluid without contributing to the glycosuria which washes out valuable electrolytes in the urine, the next step is to make good the loss of intracellular fluid By this time the blood-sugar level should have reached a fairly normal level, so the infused solution should contain glucose for the insulin to act on, as well as cellular components such as potassium, magnesium, and phosphate Omission to replace magnesium and phosphate is not reflected in any obvious clinical effects, but hypokalæmia is a real danger where the patient has become severely depleted, because the already diluted plasma-potassium tends to move into the cells under the influence of insulin Previously unexplained deaths during apparent recovery from diabetic ketosis have undoubtedly been due mainly to the cardiac effects of plasma potassium levels of under 2 m eq per litre[41,42] Potassium is best infused in a dilute solution (about 30 m eq per litre), and the infusion should be slow, in order not to risk hyperkalæmia, which can be equally dangerous It is unsafe to give potassium intravenously early in the treatment of diabetic ketosis, when its plasma-level tends to be raised already, or at any stage when the urine flow is inadequate

Severe diabetic ketosis is becoming less commo as the care of diabetics improves, but it is still a not unusual medical emergency Even small hospital should carry a stock of saline-lactate[43] and glucose-electrolyte[44] solutions, and a supply of modified Rothera's powder for estimating plasma-ketones whe the blood-sugar cannot be estimated at once

# Annotations

## AFTERMATH OF GASTRIC OPERATIONS

AN alarming picture is given by Schindler and Dagradi of the state of the gastric mucosa after operations whic create an abnormal outlet from the stomach Gastroscop was done on 368 patients after gastrectomy, gastro enterostomy, or vagal section Marginal ulcers were se in 28 of the 186 patients with a gastro enterostomy and 1 of the 148 who had undergone partial gastrectomy, in patients the ulcers gave rise to no symptoms and ha not previously been suspected The true incidence ma be higher, Meadows and Lefeber,[46] with experience over 1000 gastroscopies, were unable to see 9 anastomoti ulcers demonstrated radiographically Schindler an Dagradi also found gastritis in 84%, and in half of the patients the inflammation was severe The contro were a small group submitted either to vagal secti alone or to vagal section combined with pyloroplasty in only 1 out of 20 of these was gastritis seen, though was present in 9 of 14 others in whom gastro enterostom had been associated with vagotomy The series include only 2 cases treated by the Billroth I operation, but i both inflammation was severe It seems therefore th gastro duodenal anastomosis provides no protection whereas pyloroplasty does not damage the pylor musculature so extensively as to destroy the mechanis which prevents the unregulated reflux of what Schind and Dagradi regard as "noxious intestinal juice"

To those who see their patients regularly after oper tion, rather than the mucosa, these findings may b surprising Probably the picture is not so black as it i painted, nor the mucosa so red, for the cases seen b Schindler and Dagradi were a selected group comprisin "quite a few" seen routinely for follow up and researc purposes and a majority referred because of symptom

## THE FATE OF ASPIRIN

MANY a medical controversy has been settled as th result of an advance in a different field of inquiry Fo example, the identification of Castle's hæmopoiet principle with vitamin $B_{12}$ was due to the application of new analytical techniques borrowed from chemistry B labelling with the isotope $C^{14}$, chromatographic separa n and measurement of ultraviolet fluorescence and tical density, Mandel et al [1] have now answered the estion what happens to aspirin in the body? This estion is important because the analgesic properties aspirin are thought to reside in the whole substance l to be lost on hydrolysis. Mandel et al have shown at after ingestion of aspirin both aspirin itself and icylic acid appear in the plasma The highest concen tion of aspirin is reached after thirty minutes there er the level falls and after two hours only negligible ounts remain The proportion of total salicylate esent as aspirin in the plasma declines steadily and trapolation of the curve obtained by plotting this tio against time after absorption shows that at zero ne' aspirin constitutes virtually 100% of the total licylates. Mandel et al. conclude that aspirin may be sorbed from the intestinal tract unchanged, and that ich, if not all, of the salicylate present in the plasma o hours after administration may have been formed by ydrolysis of acetylsalicylic acid

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[38] Micks R H Brit med J 1948 ii 200
[39] Dumm R M Shipley R A J Lab clin Med 1946 31 1162
[40] Guest J M Mackler B Knowles H C Jun Diabetes 1952
[41] Martin H E Westover L Simonsen D G, Mehl J W Calif Med 1950 72 133
[42] Stephens F I Ann intern Med 1949 30 1272
[43] Saline lactate solution sodium chloride 5 85 g sodium lactat 3 36 g distilled water to 1 litre (sodium 130 m eq per litr chloride 100 m eq lactate 30 m eq )
[44] Glucose-electrolyte solution sodium chloride 1 17 g dipota sium hydrogen phosphate 0 87 g potassium chloride 1 49 g water to 1 litr magnesium chloride 0 24 g glucose 50 g (sodium 20 m.eq per litre, potassium 30 m eq chloride 45 m.eq phosphate 10 m eq magnesium 5 m eq glucose 5%)
[45] Schindler R Dagradi, A E Surg Gynec Obstet 1955 100,
[46] Meadows J C Lefeber E J Ann intern Med 1955 42

These findings accord with the familiar clinical observa on that the analgesic activity of aspirin reaches a ximum within half an hour after ingestion, and that e action wears off within two hours

## TRIGGER FINGER

STENOSING tenosynovitis is a constriction of the ndon-sheath usually associated with changes in the ndon itself producing snapping on extension or flexion a digit, or particularly in children gross limitation of tension Fahey and Bollinger [2] have investigated this ndition In the child the flexor pollicis longus is the ly tendon commonly affected and the disorder is casionally noticed at birth The thumb is usually ked in flexion and cannot be passively extended—a n which distinguishes this disorder from the adducted umb of the spastic child and which often results in a staken diagnosis of congenital contracture or disloca n In the child snapping is absent but the diagnosis ay be confirmed by the presence of a firm nodule in nt of the metacarpo phalangeal joint In adults too e thumb is commonly affected Snapping is usually e only symptom although occasionally active flexion ay be completely lost A firm nodule is always palpable the base of the thumb this nodule does not move ring flexion of the digit Of the other fingers the rd and fourth are the most commonly affected casionally both hands are involved, and Watson-Jones [3] ported the case of a child with eight fingers affected igger finger has been found in association with the re common de Quervain s syndrome [4]

Pathological changes are most prominent within the rous tendon sheath which shows fibrous tissue pro ration and degeneration; the degenerative changes lude fraying of fibres and the formation of pseudocysts of cartilage Changes in the tendon itself are more ominent in children than in adults usually producing nodular or bulbous enlargement with constriction of e tendon either proximal or distal to this swelling e cause of this disorder is obscure There is little idence of a familial association but in the child the ndition is clearly sometimes congenital In the adult e onset may be related to trauma or possibly to accustomed occupations. Men are relatively immune ich is difficult to explain since in infants the sexes e more or less equally affected

Treatment of stenosing tenosynovitis is simple and ective The tumour is exposed under local or general esthesia and a longitudinal incision made along the tendon sheath Such an incisio rees the tendon and if made laterally will not result in w-stringing There is little evidence that conservative atment is of any value or that more widespread excisic of the sheath is necessary Few operations have more sat factory results

## PSYCHOTIC CHILDREN

PLACES in mental deficiency institutions ar scarce which means that by the time a child is admitted o one a good many attempts will have been made to alle ate his mentally retarded condition: indeed, he may ot be admitted until he has proved beyond ordinary family and social care By that time it is easy to overlook the early history and to think of all such children as congenital failures O'Gorman [1] has recently discussed whether some of these cases may be the result of an early psychosis—whether they represent, in fact dementia rather than amentia. At first sight this seems to be a point of merely academic interest and indeed as far as difficulty of diagnosis understanding of psychopathology, and hopes of cure go there may not be much to choose between two such dire end results On the other hand modern psychiatry is developing more optimistic therapy for adults suffering from mental illness and fewer are relegated *at an early stage* to mere custodial care If psychosis is commoner in childhood than has generally been thought early diagnosis should offer hopes of cure for some at least Rogers,[2] in fact, has recently described how a remission (to put it no higher) was achieved in one psychotic child of 7, mainly by ensuring for him enough individual attention to keep him in touch with his surroundings and prevent him from losing himself in solitary fantasy

The idea that psychosis in childhood is not rare has been put forward by Mildred Creak [3] and other child psychiatrists here in the United States and in Europe, and the time is ripe for more concentrated research on such cases. Nomenclature is so far puzzling reflecting the difficulty observers find in arriving at a diagnosis when the disrupting factor operates early in life while development is still in progress As long ago as 1906 de Sanctis [4] used the term 'dementia præcocissima and Heller [5] (in 1908) the term 'dementia infantilis," implying an active deterioration, but these terms coincided with the then current diagnosis of ' dementia præcox Bleuler besides providing a new name threw new light on the condition he called schizophrenia and many writers since have described the disordered function and break up of personality associated with this disease —itself almost certainly not a single or unified clinical entity The fact that the pathology of schizophrenia is still a major problem for research psychiatrists should direct their attention to psychotic children for these may well be the clinical group presenting schizophrenia in pure culture as it were O Gorman s figures suggest that a sizeable proportion of cases in mental deficiency institutions may on closer scrutiny prove to belong to this group

Indeed it is perhaps time to study afresh the whole question of mental deficiency Are we justified in thinking of even congenital conditions as *necessarily* beyond remedy? Certainly few mentally defective patients are so clearly open to treatment as the cretin but Woolf et al.[6] have recently suggested that it may become possible to remedy the mental deficiency of children who excrete phenylpyruvic acid. Our notions of mental disorder are hindered rather than helped by our preoccupation with symptoms—that meagre array of distress signals which the fogged and clouded intellect

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Mandel, H G, Cambosos N M Smith, P K J *Pharmacol* 19 4 112, 495

Fahey J J, Bollinger J A J *Bone Jt Surg* 1954 36A 1200

Watson Jones R. Fractures and Joint Injuries Edinburgh, 1943

Aitken, A. I *New Engl J Med* 1945 232 105 hangs out to catch our attention Yet the very term "breakdown" invites us to look deeper—implying, as it does, a special vulnerability, a genetic factor, which has encountered a second factor, a set of adverse circumstances in the environment In our mental deficiency institutions there may be others besides psychotic children who began life with average mental capacity, and for whom the normal pattern of development was disrupted by something which happened postnatally The concept suggests opportunities for preventive psychiatry which pædiatricians and psychiatrists might explore—if possible together

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[1] O Gorman, G J *ment Sci* 1954 100, 934

[2] Rogers, J B. See *Lancet*, Jan 1 1955 p 28

[3] J *ment Sci* 1951 97 515

[4] de Sanctis S *Riv sper Freniat* 1906 32 141

[5] Heller T *Z Jugendl Schwachsinns*, 1908 2 17

[6] Woolf L I Griffiths R. Moncrieff A *Brit med J* Jan 8 1955 p 57

## IRON AS A LIVER POISON

DEATHS from overdosage of iron preparations prescribed for therapeutic purposes are distressingly numerous Some of the attractive proprietary preparations are readily mistaken for sweetmeats, and this, together with apparently special susceptibility in the young, no doubt accounts for the relatively high incidence of iron poisoning in infants and young children The three fatal cases observed by Luongo and Bjornson[1] over a period of two years in a population of a million may be a rough guide to the frequency of such poisoning

The principal clinical manifestations are vomiting followed by profound shock, coma, and death despite prompt restorative measures The depth and speed of development of shock suggests the rapid entrance into the circulation of a potent vasodilator,[2] and it is not unreasonable to relate this to the known action of ferritin an iron protein complex extractable from the liver which is thought normally to play an important part in the control of iron absorption from the alimentary canal In the presence of a massive dose of ferrous sulphate this controlling mechanism is supposed to break down—a supposition borne out by the presence of histochemically demonstrable iron in the endothelial cells of the submucosal veins of the stomach This gross excess of iron is then available to combine with the protein, apo ferritin, which is normally present in the liver, resulting in the formation of an excess of ferritin

Necropsy usually shows œdema and ulceration of the stomach associated with characteristic brown staining of the mucous membrane Apart from some pulmonary œdema and congestion of other viscera, the only organ consistently affected is the liver, but the changes have been variously described as cloudy swelling, fatty infiltration, and zonal necrosis, sometimes central and sometimes periportal The three cases reported by Luongo and Bjornson are notable for the striking periportal necrosis, which was recognisable even in the third child who survived only for about four hours The relation of necrosis to the ingestion of iron was definitely established by the production of virtually identical lesions in laboratory animals In rabbits given ferrous sulphate in solution by stomach tube, doses of less than 0 75 g per kg body-weight were apparently non toxic, but doses of 0 75–1 g per kg regularly resulted in hepatic lesions in the periportal zones Of 25 rabbits which received 1 g per kg, 6 died in a few hours, the remainder survived and were killed at intervals subsequently At twenty four to forty eight hours these rabbits had severe hæmorrhagic periportal necrosis Little evidence of necrosis remained at five to six days, but slight periportal fibrosis had developed which gradually increased, and after two weeks the lobular architecture was distorted by a fine diffuse fibrosis

Thus both clinical and experimental observations leave no doubt that ferrous sulphate in large doses produces serious liver injury The maximal severity of the lesions in the periportal as opposed to the centrilobular zones suggests that the hepatic cellular damage is due to the direct toxic effect of the metal and not to impaired intrahepatic circulation, such as is unquestionably found in severe shock, but the shock usually associated with ferrous sulphate poisoning may enhance the direct toxicity, as with many other liver poisons including chloroform and carbon tetrachloride

Two forms of hepatic cirrhosis associated with heavy deposits of iron in the liver are now recognised, hæmochromatosis in this country, and the nutritional cirrhosis described by the Gillmans[3] in South Africa The pathogenesis of both these types is still far from clear It is essential to investigate the various factors, nutritional and environmental, which might modify the susceptibility of the liver cells to the toxic action of iron, in order to clarify the rôle, if any, of the iron deposits in the genes of cirrhosis in these siderotic livers

## RICE

RICE, wheat, and maize (corn) are the three main cere of the world Of these, rice is quantitatively the mo important, for it is the staple food of over half the peop of the world In the densely inhabited rice grow countries of Asia, rice provides 70% or more of the tot calories in the daily diet of most of the population F the poor peasants and the rapidly increasing indust workers, both the quantity and the quality of their r are all-important In 1948 F A O published a sm monograph setting out the nutritive value of differ forms of rice in relation to other foods usually consum in these countries and to the over all dietary needs of th people This monograph at once became popular a was twice reprinted A new edition[4] incorporates t results of recent investigations

Rice may lose much of its original nutritive val during milling, washing, and cooking In this it resemb wheat and other cereals, but the extent of the losses a their effect on the over-all value of the diet are usua much greater than in wheat eating countries In the ru districts most of the rice is still milled by the women the household This is a wearisome task, but hom pounded rice nearly always retains most of the nutrien in the original grain Rice mills are now spreading in most of the small towns and larger villages Since t war little mills have become popular in some countr notably Thailand, they are driven by small petr engines, and the capital required for their purchase not beyond the means of the headman of even a v small village Almost all the rice consumed in towns h been through the mills Most samples of milled rice not satisfactory foods, especially when the rice prov a large proportion of the total calories in the diets. B several important advances have been made which m have great repercussions on the milling processes

Hinton,[5] in England, has studied the distribution o vitamins in the various parts of the rice grain, wh can be separated by microdissection He found th the scutellum, which is a small structure between th embryo and the endosperm, contains about 50% of th total aneurine in a rice grain, although it accounts fo only 1 5% of the total weight The scutellum is also ric in nicotinic acid and riboflavine Clearly a milling tech nique that retained the scutellum attached to the grai would provide a rice of much superior nutritive properties So far the problem of devising a milling process that wi remove enough of the pericarp to provide an acceptabl rice and yet retain the scutellum does not seem to hav been solved

The fortification of refined wheat flours with vitamin and minerals has been practised for many years in th U S A and elsewhere Similarly rice can be fortified b preparing a rice premix and adding this to ordinary whit

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[1] Luongo, M A Bjornson S S *New Engl J Med* 1954 251,

*J Path Bact* 1952 64 467

[3] Gillman J Gillman T *Arch Path (Lab Med)* 1945 40 2

[4] Rice and Rice Diet A Nutritional Survey F A O Nutriti Study no 1 Rome 1954 Obtainable from H M Stationery Office Pp 93 3s 9d

[5] Hinton J J C *Brit J Nutrit* 1948, 2, 237

. The premix consists of milled rice impregnated with olution of the required vitamins and minerals the nts are then provided with a coat insoluble in cold er This premix is mixed with ordinary milled rice ally in the proportion of 1 to 200 by means of a ler at the mill Extensive experiments with enriched carried out in the Philippines in 1948–50 [6] showed t in a rice-eating country vitamin enrichment could g about a striking reduction in the incidence of iberi. An international team which visited the ilippines appreciated that enrichment of rice had led substantial improvements in nutrition [7] They were o impressed by the many difficulties that might prevent e effective application of an enrichment policy in other ble countries.

Parboiled rice obtained by pounding or milling paddy ich has been steeped in water steamed and subse ently dried, has long been known to be unassociated th beriberi Parboiled rice can be milled to a high gree without serious loss of thiamine or other water able vitamins Parboiling as practised in the home d in many rice mills is an unstandardised process d the flavour of most parboiled rices is unacceptable those unaccustomed to it But plants for parboiling under standard conditions which yield a good quality duct that is more generally acceptable have been eloped in the past twenty years. Such processes, wn as 'conversion or malekising of rice are tected by patents But there is no indication of any ral movement towards the adoption of parboiling in ntries where this is not already habitual

Meanwhile beriberi remains a common disease If in ny countries, such as Japan and the Philippines the dence appears to have fallen in others such as ailand, there is evidence of some increase We have knowledge to eradicate completely this disease, yet have not been able to do so The problem is no longer mical or medical. Engineering sociology and econo s are the disciplines through which the solution must e Beriberi is of course not the only deficiency ase prevalent among poor rice eaters Keratomalacia, atitis, glossitis cheilosis and burning feet' are mmoner than among wheat-eating populations Nor the rice mills the sole or even the most important the nutritional problems of the East Typical rice s contain too much rice in proportion to other foods s imbalance can be corrected only when the yields ice per acre have been increased and land has thereby n liberated for alternative crops and animal husbandry re is reason to believe that in many areas more land ld soon be made available for other cereals, pulses ns and vegetables but it seems unlikely that in any e-eating country the supply of milk meat and eggs ld be substantially increased in the immediate future re the technical problems are agricultural but culture must be related to the physiological needs of e people These can be accurately assessed only by ical and biochemical studies The national nutritional mittees that have been formed in so many countries the East are mainly concerned in coördinating research k in fields involving different academic disciplines, l in husbanding limited resources both of finance and man power for the study of problems which seem to r the greatest chances of practical solutions In eral countries there are so many urgent broad blems requiring an understanding of more than one demic discipline that very few can afford to allow ny of their experienced research workers the luxury a secluded academic life The F.A O monograph on ce and Rice Diets sets out clearly many of these broad blems in a practical and concise way

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Salcedo J., Concepcion, I Guerrero A F Pascual F F Valenzuela, R. C. *J Nutrit* 1950 42 501

Rice Enrichment in the Philippines F.A O Nutritional Study No 12. Rome 1954

## PROPHYLAXIS IN STREPTOCOCCAL EPIDEMICS

MOST, if not all strains of group A hæmolytic strepto cocci are sensitive to penicillin Apart from its usefulness in the treatment of streptococcal pharyngitis,[1] penicillin has special value in modifying the epidemiology of streptococcal infections, it is, for example, already widely used to protect susceptible people against the repeated attacks of streptococcal upper respiratory disease which are related to recurrences of rheumatic fever [2] Another aspect of prophylaxis—the prevention of rheumatic fever in large military populations of young adults—has been given much more attention in the U S.A than in this country

Workers at the Warren Air Force base have shown by their extensive observations [3,4] that the incidence of first attacks of rheumatic fever in adults may be reduced by more than 90% when the initial group A streptococcal sore throats are properly treated with penicillin In such communities another approach is to administer penicillin prophylactically to every person at epidemic times, with the aim of preventing both strepto coccal infections and their rheumatic sequelæ Seal et al [5] have investigated the epidemiological effect of such action in three regiments of Naval recruits The numbers at risk were large—each regiment was over 2000 strong—and 98% of the men received oral prophylactic penicillin for two weeks beginning when weekly hospital-admission rates for proved group A streptococcal infections were slightly over 20 per 1000 Two doses of penicillin were used—either 50 000 or 500 000 units a day—and the differences between the epidemiological effects were pronounced 50 000 units a day greatly reduced the admission rate for streptococcal infections but admis sions rapidly reverted to the previous high levels after prophylaxis was discontinued—probably because (as was shown) this dosage did not materially affect the carrier rate for the organism or alter the distribution of prevalent serological types But this dosage did sig nificantly reduce the subsequent admission rate for rheumatic fever 500 000 units daily had a more pro nounced effect The admission rate during prophylaxis dropped nearly to zero and the number of carriers fell sharply The prevalence of specific serological types was altered both in carriers and in cases of streptococcal infection after the prophylactic course and after a period there were no further cases of rheumatic fever Six weeks after the end of the prophylactic course there was a second outbreak of streptococcal infection this time due to different serological types Seal et al give cogent reasons for their belief that this epidemic was a true reinfection of the population from outside sources and the outbreak was readily controlled by a further prophylactic course of 500 000 units daily

The lessons from this valuable study seem to be these Intermittent prophylaxis with oral penicillin at times of epidemic streptococcal infections is in military com munities, both effective and practicable The epidemio logical result of such prophylaxis is related to the dosage of penicillin used 500 000 units daily significantly reduces the streptococcal morbidity rate and the distri bution and prevalence of this organism in the population Most carriers are freed of their streptococci by this régime though it cannot, of course influence subsequent reinfection with new strains But perhaps the most important effect is the reduction in the incidence of rheumatic fever

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[1] See *Lancet* 1953 i 285

[2] Stollerman G H *Amer J Med* 1954 17 757 See also *Lancet* March 5 1955 p 496

[3] Denny F W., Wannamaker L. Brink, W R Rammelkamp C H., Custer E A *J Amer med Ass.* 1950 143 151

[4] Wannamaker L W., Rammelkamp C H., Denny, F W., Brink, W R Houser, H. B Hahn, E O Dingle J H *Amer J Med* 1951 10 673.

[5] Seal J R., Mogabgab, W J., Friou, G J Banta J E *J Lab clin Med* 1954 44 831

# Social and Biological Factors in Infant Mortality *

## V. MORTALITY IN RELATION TO THE FATHER'S OCCUPATION

### 1911-1950

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THIS paper is a historical study of the mortality of children of men in different occupations Reports of the General Register Office relating to the censuses of 1911, 1921, and 1931 are used, together with data for 1939 collected for the projected census of 1941, and some results from the present inquiry for 1949–50 [47 49 50 53] Eight occupation groups will be mainly considered No such information is available before 1911, and no other occupation groups can be followed through all five periods The classification of occupations (and therefore the composition of the groups) varies a little in the different years, which makes for difficulties in comparison, and there are also some slight changes in the definitions of the mortality-rates Such points, however, are not considered important in the present context, they will be dealt with in the final report

*Occupation Groups Considered in this Analysis*

The social class to which the group is now assigned is given in parentheses

A *Professional Workers* (I) —All the occupations in social class I—e g, medical practitioners, consulting engineers, administrative Civil Servants The higher ranks of business are represented here also, but they form a small minority of the group

B *Farmers* (II) —Farmers and their relatives, land and estate agents the great majority simply described as "farmers," which includes "smallholders"

C *Teachers* (II) —Including university professors and lecturers

D *Clerical Workers* (III) —Clerks, secretaries not described as "company secretaries," office machine operators, &c

E *Textile Workers* (III and IV) —Skilled and partly skilled workers in the textile industries

F *Miners* (III) —Hewers and getters, and subordinat superintending staff the great majority being hewers and getters in *coal* mines

(IV) —Partly skilled workers underground and on the surface in mines the great majority in *coal* mines

G *Farm Workers* (IV) —All agricultural workers apa from farmers (social class II) and market gardeners, nurser men, &c (who are in social class III)

H *Building Labourers* (V) —Builders', bricklayers, plasterers', and masons' labourers, and other unskilled worke in building (mainly "navvies")

All legitimate births, single and multiple, are includ in the analysis Throughout, "occupation" refers to th occupation of the *father* of the child, no information i available about any gainful employment of the moth (and wife) [46] Father's occupation is thus an indicat of the social economic environment of the family Sometimes the father's occupation determines t physical environment also, since certain occupatio (e g, coalmining or agriculture) are tied to spec localities, and others (e g, textiles) are concentrated particular areas Findings will be reported for mortalit as a whole, in keeping with the design of the stud consideration of separate causes is postponed to a lat paper

### Results

Table I and figs 1 and 2 show the neonatal and po neonatal mortality-rates for the various occupat groups from 1911 to 1950 The rates vary materi with the occupation of the father To recognise this, it necessary only to compare coalminers' or textile work children with those of farm workers or teachers T post neonatal rate is more sensitive to the father occupation than the neonatal rate

*Uniform Decline in Occupation Groups*

Following the post-neonatal rate for the individu occupation groups, it can be seen that, for this rapi falling rate, there is a *continuous decline* in each gro

TABLE I—SECULAR TREND OF INFANT-MORTALITY RATES, 1911–1950 OCCUPATIONS AND SOCIAL CLASSES OF TH FATHERS COMPARED LEGITIMATE BIRTHS IN ENGLAND AND WALES

| — | NEONATAL DEATHS (at ages under 4 weeks) per 1000 live births | | | | | POST NEONATAL DEATHS (at ages 4 weeks–1 year) per 1000 live births | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 1911 | 1921 | 1930–32 | 1939 | 1949–50 | 1911 | 1921 | 1930–32 | 1939 | 1949–5 |
| *Father's occupation* | | | | | | | | | | |
| A Professional workers | 26 8* | 23 4 | 21 7 | 18 9 | 13 5 | 28 3* | 15 0 | 11 0 | 7 9 | 4 9 |
| B Farmers | 34 8 | 29 7 | 29 3 | 28 7 | 17 8 | 39 4 | 21 5 | 17 0 | 11 8 | 6 5 |
| C Teachers | 26 0 | 19 5 | 26 8 | 20 8 | 12 0† | 31 5 | 22 1 | 10 3 | 8 1 | 4 6† |
| D Clerical workers | 32 7 | 26 7 | 26 1 | 23 3 | 15 5 | 48 5 | 24 5 | 15 9 | 11 8 | 6 3 |
| E Textile workers | 44 4 | 39 5 | 38 0 | 34 3 | 18 6† | 103 7 | 50 8 | 30 8 | 19 5 | 14 1† |
| F Miners | 46 3 | 41 7 | 38 6 | 33 1 | 22 0 | 113 7 | 63 0 | 43 3 | 32 4 | 20 5 |
| G Farm workers | 36 5 | 34 2 | 31 7 | 28 4 | 19 0 | 59 6 | 33 4 | 20 5 | 19 8 | 10 0 |
| H Building labourers | 37 9 | 35 7 | 27 9 | 31 0 | 20 5 | 100 6 | 57 3 | 36 9 | 27 0 | [illegible] |
| *Father's social class* | | | | | | | | | | |
| I Professional | 26 8* | 23 4 | 21 7 | 18 9 | 13 5 | 28 3* | 15 0 | 11 0 | 7 9 | 4 9 |
| II Intermediate | 34 8 | 28 3 | 27 2 | 23 4 | 16 0 | 63 2 | 27 1 | 17 8 | 11 0 | 5 9 |
| III Skilled workers | 39 6* | 33 7 | 29 4 | 25 4 | 17 8 | 85 8* | 43 2 | 28 2 | 19 0 | 10 5 |
| IV Partly skilled workers | | 36 7 | 31 9 | 27 7 | 19 9 | | 52 7 | 34 9 | 23 7 | 14 1 |
| V Unskilled workers | 42 5 | 36 9 | 32 5 | 30 1 | 21 9 | 110 0 | 60 2 | 44 6 | 30 0 | 17 9 |
| ALL CLASSES AND OCCUPATIONS | 39 1 | 33 9 | 30 2 | 26 4 | 18 2 | 85 8 | 45 3 | 31 4 | 21 0 | 11 1 |

* The figures for 1911 require care in interpretation In 1911 there were 8 classes of which VI VII and VIII were, respectively textile workers miners and agricultural workers For the purpose of this study classes III IV VI VII and VIII of 1911 were amalgamated t form one large class corresponding to a combination of III and IV of later years Again class I of 1911 included many occupations classifi from 1921 onwards in classes II and III In this study "class I" for 1911 includes only those occupations which were also in cla in 1921

† 1950 only

*Numbers* —Space forbids separate tabulations of the numbers of deaths and births in each occupation group in each year Howev except for teachers, the number of deaths is always greater than 100 and the number of births greater than 7000 The smallest number of deaths is 31 for the post neonatal rate of teachers children in 1939 and the denominator never falls below 2700

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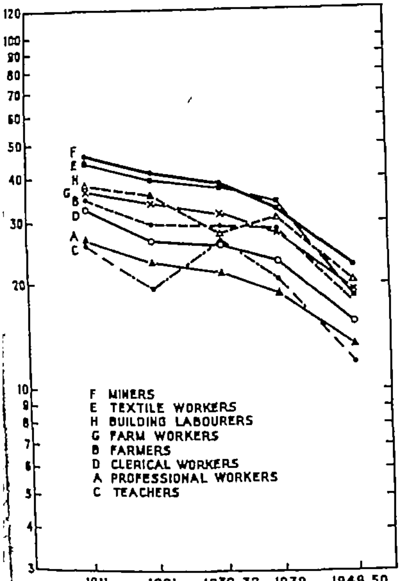
* A series of articles reporting an inquiry made jointly by the Social Medicine Research Unit (Medical Research Council) and the General Register Office The articles [1–4] were prepared by the Unit in collaboration with the General Register Office, and have been approved for publication by the joint working party responsible for the inquiry



1—Secular trend of neonatal mortality-rates 1911–1950 : occupa- ns of fathers compared. Legitimate births in England and les.

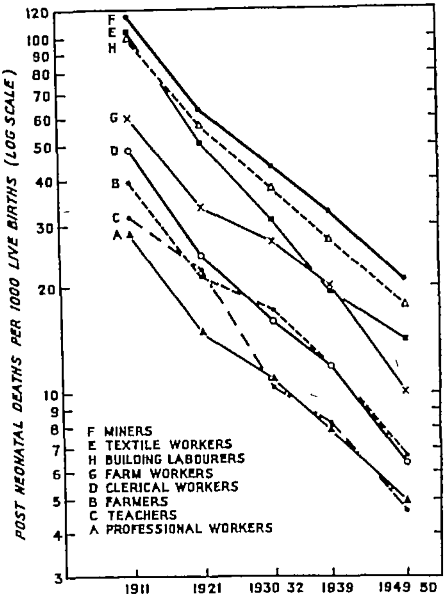


Fig 2—Secular trend of post-neonatal mortality-rates 1911–1950 : occupations of fathers compared. Legitimate births in England and Wales.

n 1911 to 1950 (fig 2) The neonatal rate which not fall so rapidly (fig 1) shows two exceptions—ers and building labourers—where there are ularities though the general trend even for these same. Moreover the fall for each occupation group *about the same proportion* Table II shows the per ge change in the mortality rates over the whole od for each group The fall in the neonatal mortality during the forty years varies from 40 to 58% of 1911 figure ; the fall in the post neonatal rate from 67% The similarity of experience is illustrated gs. 1 and 2 where because a logarithmic scale has used, occupation groups whose rates have fallen by l proportions will be represented by parallel lines both figures it can be seen that the proportionate ine over the period as a whole has been fairly similar all the groups. That is to say the very different social riences of these groups during forty eventful years ative ease of deprivation and of stress[10] are not ted in their infant mortality Miners for example ered a steady improvement in mortality through prosperity of 1911–21 the vicissitudes of 1921–31, ump of the 1930s and the later recovery Clerks economic history in no way so chequered and ly if anything losing ground in comparison d very much the same decline There does not r to be anything in the choice of occupations which be responsible for these trends The groups are ge and fairly homogeneous Other occupations hich there is less complete information during 50— dock workers ' also a homogeneous group transport workers and armed forces other than s, much less homogeneous groups—show the same

consequence of the rough equality of decline among various occupation groups is that differences between are just as great relatively at the modern level of infant mortality as they were when the rates were very much higher forty years ago In 1911 for example, the post neonatal mortality rate of the children of miners (113 7 per 1000 the worst rate in the eight groups studied) was four times as high as the lowest (children of professional workers, 28 3). In 1949–50 the rate for the miners children (20 8 per 1000) was still about four times as high as the rate for the children of professional men (4 9) and more than four times higher than the lowest rate in this period (the children of teachers 4 6) † The gap between the highest and lowest rate was thus if anything somewhat greater in 1949–50 than in 1911 ‡ However the increase is slight and it may possibly be accounted for by minor changes in the composition of the groups.

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† This method of comparison (expressing the highest rate in terms of the lowest at the beginning and at the end of the period) does not of course use all the data. It is interesting therefore to compare the coefficients of variation of the rates in the eight groups during the period :

*Coefficient of variation of the eight mortality rates*

| | *1911* | *1921* | *1930–2* | *1939* | *1949–50* |
|---|---|---|---|---|---|
| Neonatal mortality rate | 0 10 | 0 23 | 0 18 | 0 20 | 0 19 |
| Post neonatal mortality rate | 0 50 | 0 18 | 0 48 | 0 19 | 0 55 |

This alternative measure of the importance of the *differences* in the rates is remarkably constant

It is interesting too that the decline in the neonatal and post neonatal rates for all occupations taken together (i.e., the national averages) is on the high side compared with the decline for most of the eight individual groups This is because of the considerable increase in size over the forty years, of the groups with favourable rates (professional workers and clerks, for instance) and the decline in size of the groups with unfavourable rates (such as textile workers and miners)

‡ Titmuss[11] gives a detailed discussion of the changes in the gap in infant mortality rates between the social classes from 1911 to 1930–32

TABLE II—THE FALL IN INFANT MORTALITY RATES, 1911–50 OCCUPATIONS OF THE FATHERS COMPARED LEGITIMATE BIRTHS IN ENGLAND AND WALES

| Father's occupation | | The percentage fall 1911–1949/50 | |
|---|---|---|---|
| | | Neonatal deaths (at ages under 4 weeks) | Post neonatal deaths (at ages 4 weeks–1 year) |
| A | Professional workers | 50 | 83 |
| B | Farmers | 49 | 84 |
| C | Teachers | 54 | 85 |
| D | Clerical workers | 53 | 87 |
| E | Textile workers | 58 | 86 |
| F | Miners | 51 | 82 |
| G | Farm Workers | 48 | 83 |
| H | Building labourers | 46 | 83 |
| ALL OCCUPATIONS (not only those shown above) | | 53 % | 87 % |

The emphasis on the *proportionate* decline of the rates, and the rough equality among occupations in this respect, must not obscure the fact that the decline in *absolute* numbers of deaths, and the consequent saving of life, has been greater among the children of men in occupations with high rates than in those with low (This statement of course has nothing to do with the fact that some occupation groups are larger than others The comparison is made per 1000 births in each "occupation") A drop in the post neonatal mortality rate of miners' infants from 114 to 21 means the saving of 93 deaths among every 1000 infants—i e , of almost 10 per cent of the children born The corresponding decline among professional workers, from 28 to 5, means the numerically smaller saving of 23 deaths per 1000 born In this sense, therefore, it would not be true to say that all occupations have benefited equally , the occupations which had (and still have) the worst record have benefited the most—and very much so It is from the point of view of ætiology—of what has caused the decline, and what causes the differences between social classes or occupations—that the proportional approach seems correct

*Comparison with the Decline in the Five Social Classes*

The rough equality of decline demonstrated for the occupation groups occurs also when the occupations are grouped together into the conventional five "social classes"[54] (table I) Can anything more be learnt from the present findings about occupation groups than from the broader study of social classes ? Both are aggregates of men in a number of particular jobs , the allocation to social class being mainly "based on general standing within the community"[51]

The order of the occupation groups, when arranged according to their infant mortality, may at first sight appear very similar to the order that would be obtained by arranging them in the social classes to which they are allocated , but it differs in two ways There are occupation groups within a class whose rates are not at all similar to the rates of other occupations within the class , and this has been true since 1911 Moreover, there are occupation groups within an industry, and normally classified to different social classes, whose rates have been similar throughout the period

Both these points are illustrated in fig 3, where it can be seen that the post neonatal rate for children of *miners* in social class III is very different from that for the children of *clerks* of class III Moreover, the rate for miners' children is much the same whether the fathers are "skilled" (in social class III) or "partly skilled" (in class IV), it has been similar to that of class V throughout the period This dismal record is true also of the neonatal rate

Analysis in terms of social class, then, masks considerable variations within the classes This must be expected when such large generalisations are made thousands of real life occupations have to be graded into only five abstract and often, of necessity, arbitrary "classes" But instances of occupation groups which differ from their class fellows may also provide useful clues to ætiology Thus, miners in social class III ear more than miners in social class IV, but their infant fare as unfortunately—it may be because they live i the same often rather isolated villages and share man attitudes and traditions, the same "culture"[38] Th persistently unsatisfactory rates in the infants of text workers, compared with other skilled and partly skill workers, points to a local situation needing special stud (and related, some have thought, to the high rate employment outside the home of *wives* of text workers)[24 46 59] The similarity between the rates in th children of farm workers (allocated to social class and probably rightly so in terms of real wages) and th rates of children in social class III is another illustrati of the superior health of the agricultural populati The closeness of the record in the children of cle (social class III) to that of teachers' children (social cl II) may point to common "white collar," "midd class" standards

### Comment

One fact stands out from recent social studies of inf mortality,[54 25] including the present one—the rem able similarity of the decline among various social gro There has been no narrowing of the social gap in in mortality , if anything it may have widened sligh This finding was unexpected At any rate, someth different was hoped for in the 1930s Infant mortal by tradition and on repeated showing from Farr, thro Newsholme and till today, is highly sensitive to so conditions Different sections of the population h been very differently affected by recent social chang and in the last twenty years, anyhow, full employme higher real wages, and expanding social services have

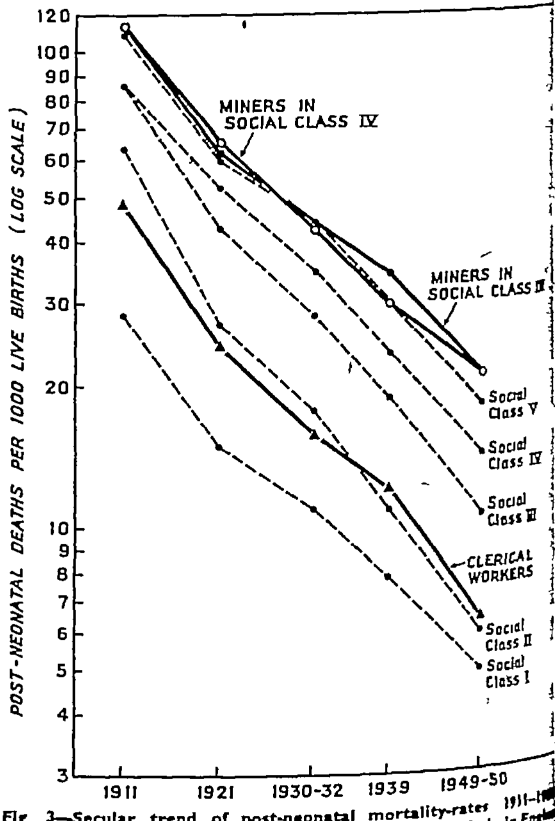


Fig 3—Secular trend of post-neonatal mortality-rates 1911–1 children of miners and clerks compared Legitimate births in Eng and Wales

1911 rates are adjusted See footnote to table I o relatively greater improvement in the situation of the uilding and dock labourers of social class V and the iners in class III, for example than of clerks or pro ssional people As indicated however this different perience is not reflected at all in the infant mortality tes (and this despite the fact that there was so much re room for improvement in the worse rates) Clearly is important to consider why

Some evidence of the recent levelling of social-economic andards may be mentioned Weekly wage-earnings have reased more since before the war than salaries and ges in "depressed" industries and of unskilled workers re than others. When allowance is made for direct taxation d changes in retail prices male wage-earners were some % better off on average in 1950 than in 1938 salary-earners about held their own; rentiers were worse placed [9] "In 1936 17 7 per cent of the people of York (a repro ntative city) were below Rowntree's poverty line [48] but in 50 only 1 7 per cent Yet in 1936 [the real amount of ources actually used by the population] was as great as, obably slightly greater than the amount in 1950 This ngly suggests that the whole improvement recorded in eys such as Rowntree's had been effected by a *redistribution* the resources available for consumption (including social vices) All the [old and newer] welfare schemes are ely equalitarian Education the health service d and other general consumer subsidies all represent portionately greater additions to the money incomes of r men than of rich, of family men than of the childless [9, 44] Whatever has happened among others the diet of the er sections of the population has improved substantially re the 1930s. Weekly expenditure on food per head in the 1930s averaged from about 4–5s in the poorest groups, 1s and up to 17s (over three times as much) in the most prosperous.[9, 44, 48] Corresponding figures in 1950 would be of the order of 15s ranging to 21s (less than one and a half times)—a narrowing of the gap by two thirds i.e. this substantial reduction in social class differences was achieved largely by the levelling up of expenditure on the part of the lower class. [9] (If information about expenditure on clothing were available the approximation of the social classes might we fancy be even more obvious; but we have been unable to trace the necessary data) The poorer have also benefited particularly from various family aid policies, such as child allowances, from housing subsidies and rent control There is evidence that the worst housed in terms of overcrowding have registered the greatest improvement since 1931 [51]; though there is no such information about household conveniences and amenities.

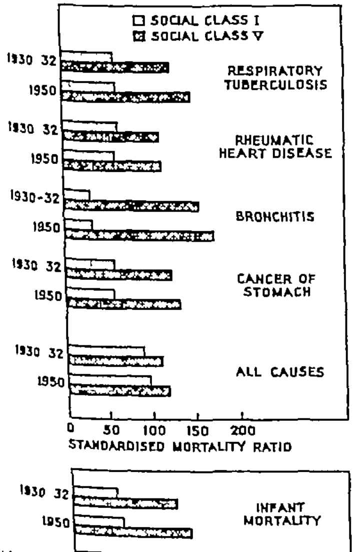
All in all there is no doubt that comparing 1940–50 with the 1930s for example there has been some levelling of standards of living What has happened since 1950 does not concern us now

*The Social-class Gap in Adult Mortality*

In passing, it should be noticed that this similarity of decline in mortality rates among population groups with different recent social experiences is not limited to infant mortality In all the major conditions from which adult men in social class V had a higher death rate in 1930–32 than social class I the gap was as big in 1950 as twenty years before—and if anything slightly wider [50, 54] Fig 4 illustrates this for four causes of death classically associated with poverty § Tuberculosis and rheumatic heart-disease have shown substantial over all reductions in mortality during recent years.[55] In bronchitis and cancer of the stomach this is not so—which difference in behaviour does not seem to have affected the trend either way The record social-class differences in the mortality of married women is much the same as for the men ‖ In trying to understand the recent social history of infant mortality therefore regard should also be paid to the more general phenomenon The persistence of the gap between the social classes in infant mortality is unlikely to be entirely explained by factors concerned only with childbearing or the care of infants though, for the present consideration must be focused on these

*Maternal Age and Parity During the Period*

Another preliminary point needs to be made The ages of the mothers and size of families (which have been shown to be related to the infant mortality) may have changed in the different social classes and occupation groups in such a way that any tendency for the gap to narrow because of social levelling has been counter balanced There is no direct evidence on this point but such information as there is tends to show that there can be no such explanation [2, 11, 18, 20, 31, 32, 40] In the only direct comparison which can be made with an earlier



4—Differences between social classes I and V in mortality of adult ales: 1930–32 and 1950 compared for several causes of death. (Infant ortality is also shown.)

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§ STANDARDISED MORTALITY RATIOS. MEN AGED 20–64 ENGLAND AND WALES

| | | Social Class | | | | | |
|---|---|---|---|---|---|---|---|
| | | I | II | III | IV | V | V/I |
| Respiratory tuberculosis | 1930–32 | 61 | 70 | 100 | 104 | 125 | 205 |
| | 1950 | 61 | 82 | 103 | 95 | 142 | 233 |
| "Rheumatic heart disease" | 1930–32 | 65 | 92 | 97 | 111 | 112 | 173 |
| | 1950 | 61 | 87 | 103 | 102 | 114 | 187 |
| Bronchitis | 1930–32 | 31 | 57 | 91 | 124 | 160 | 503 |
| | 1950 | 33 | 63 | 97 | 103 | 172 | 521 |
| Cancer of stomach" | 1930–32 | 59 | 84 | 98 | 108 | 124 | 210 |
| | 1950 | 57 | 67 | 100 | 114 | 132 | 232 |
| All causes | 1930–32 | 90 | 94 | 97 | 102 | 111 | 123 |
| | 1950 | 97 | 86 | 102 | 94 | 118 | 122 |
| Infant mortality rates (% of all classes) | 1930–32 | 53 | 3 | 94 | 105 | 126 | 238 |
| | 1950 | 61 | 76 | 96 | 113 | 139 | 228 |

(It will be noticed that in 1950 in the mortality from respiratory tuberculosis—and possibly from rheumatic heart-disease—there is the same "W" trend that appeared for the first time in mortality from all causes in 1950)

‖ Among the adults, very interestingly in the diseases associated with prosperity rather than poverty and showing higher death rates in the upper than lower classes—coronary heart-disease and diabetes in men and cancer of the breast for example—the gap in mortality between social class I and social class V has tended to narrow in recent years.[50, 54]

" Males aged 20–64 in England and Wales In 1930–32 the ures for cancer of the stomach include cancer of the oeso gus, and the figures for rheumatic heart-disease include ronic endocarditis." Examination shows, however that se inclusions do not invalidate the comparisons made in the gram. For infant mortality the rates are expressed as a rcentage of the rate for all classes in each period

period, namely between the stillbirth rates in 1939 and 1949, correction for differences in age and parity shows no narrowing of the gap between the social classes

STILLBIRTH RATES STANDARISED FOR MOTHER'S AGE AND PARITY[3]

| Year | Social Class | | | | |
|---|---|---|---|---|---|
| | I | II | III | IV | V |
| 1939<br>1949 | 23 4<br>14 3 | 29 3<br>18 9 | 33 2<br>21 5 | 36 3<br>23 2 | 37 2<br>26 0 |
| % decrease | 39 | 35 | 35 | 36 | 30 |

Differences nowadays between social groups in the ages and parities of the mothers affect the over all infant-mortality rates of the groups very little The reasons for this have been discussed,[3,4] and are likely to have been as applicable in 1911 as they are now This last statement is supported by examination of the data for the fertility of the wives of men in different occupations in 1911,[48] and the same report also includes some mortality data for their children The Family Census has recently shown moreover, that, so far as the comparison can be made, family sizes were reduced during the period under observation by about 30% among all the occupational groups they studied[13]

*Three Suggestions*

Three lines of speculation about the recent social trends of infant mortality can be suggested the *first* is concerned with time lag in the improvement of health as a result of social improvements, the *second* approach deals with the changing composition of social groups, the *third* emphasises that the whole question—a crucial one for contemporary social medicine—is still open

1 *Time lag*—Very little is known about patterns of family expenditure in different sections of the population But on the available evidence it cannot be assumed that money devoted to the care of the family increases among all classes as soon, and as much, as money wages increase ¶[45,57,60,66] There may be delay therefore in the expression of such rising standards of living in better health There may be a lag also in the knowledge of, use by, or availability to, families in social classes IV and V of new scientific advances, of services, and of facilities, compared with classes I and II The better educated, that is to say, may have benefited more from recent medical progress than others[62] The disappointing take up of "welfare" vitamins may be recalled here[36] The period being studied, 1911–50, saw the great expansion of personal preventive medical services But in 1946 it was found that antenatal services were used most by the "middle classes"[35] A further survey in 1953 confirmed this observation, and showed that the greatest improvement since 1946 had been among the wives of skilled manual workers, not those in classes IV and V[30] This may be an example of "cultural lag," of family traditions (the influence of grandmother?) which might be counteracting the benefits of community provision There may be an illustration here also of the general phenomenon of resistance to change—that it is easier to continue along existing lines than to learn and change, which may explain the continuing low rates of the clerks and high rates of the miners Then, in longer terms, capital assets may be more important than current income in the needs of maternal and infant well being, and hence in determining the death rates (By "capital" such goods are meant as housing and i amenities, and education) These are slower to chang with an increase of real wages and the passage of leg lation, than expenditure on immediate needs which ca rapidly rise (and fall)[40,63] There has been some narrowin of the gap in respect of capital goods such as housing but the equalising effects of the Education Act, 194 may take a long time to show in infant mortality I may well be that as the gains of full employment and t Welfare State are consolidated, the "capital" of t sections of the population which were poor in the 19 will increase, and they will begin to overtake the infa mortality record of the more prosperous instead of mer keeping in step with it Finally, the notion of "generati mortality"[21,34]—that the levels of death rates dur later life of a population cohort are settled early in life—might possibly be extended here, in particular the rates of stillbirth and neonatal death among wo the foundation of whose own healthiness and unhealt ness was laid down during years of economic depre and before the most recent and substantial so advances

The upshot of this line of speculation is simply t the time factor may be all important in understanding t social history of infant (or any) mortality We may on the wrong time scale in expecting that the Wel State should already have had specific effects on class differentials in infant mortality The slow narro of the gap between income groups in the stature of t school-children[5] may thus be illustrating the signific of the time scale in physiological terms In term morbidity we do not have the necessary data, but should be very surprised if social class analysis of org disease in childhood—of nutritional anæmia in infant infantile rickets (and for that matter, of rickety p in young adults), and of such conditions as chronic o media did not show a narrowing of the class gap over past twenty years i e, quite rapid changes The re history of rheumatic heart disease may be relevant to problem as it relates to mortality The difference bet social economic groups in young people's mortality f this condition is now less than before the war[39,55], tho in adults, as said previously, there is still no cha The rates in all the younger groups are now very lo beginning, it may be, to approach the minimum possible with the present genetic constitution of population?

2 *Population movements*—For a second specula the composition of different sections of the popul needs to be considered, because among the many th that may be happening is a peculiar balancing of so and biological forces within the various classes. Gr movements have taken place between the social cla in recent years About half the adult men nowada there is reason to believe, are in a different class fr their fathers[12,29] If this inter class movement is rel to health, the sick tending to decline in status and healthy to rise, processes opposing the effects of econo levelling could be postulated That this suggestion pertinent can be supported by much indirect evide (*a*) that the healthy do, selectively, leave populatio (migration from the "depressed" areas in the inter years, for example), and (*b*) that the unhealt similarly, join populations (changing to different occu tions—because of heart disease, for instance) Th questions are among the staples of social medical resea and proper consideration of them would take us too afield[7,14–17,22,23,26,27,42,43,55]

An original explanation along such lines of re class trends in infant mortality has been propound from the current Aberdeen study of primigravid It has been shown there that the women whose fat were in social class III, but who themselves have marr men in social classes IV and V, have higher "obstetric death rates and a higher proportion of premature bab han women who have changed in the opposite direction—e., have moved from classes IV and V to class III It ppears, too that women who thus change their social ass at marriage tend to have characteristics in common ith the women in the class to which they transfer rather an the class from which they come—including characristics which affect the "obstetric" or "perinatal" ortality rates, such as general healthiness physique d education.[19] Since social class V has been shrinking size during recent years, such a process could well be mulative and counteract the benefits of social vances. (The theoretical bridge between this notion d "generation mortality" is readily apparent) The *temporary* environmental factors—the situation into ich the women have moved—need to be considered wever, as well as host factors and they must be portant The question should be clearer when alyses are available for post neonatal mortality with apparent special sensitivity to current social conditions

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¶ A pointer to contemporary values, of the kind that needs investigation is this quotation

> An example of the commercial effects of working-class prosperity is the rise of the specialised 'baby shop' In 1939 there were perhaps two hundred shops [in London] selling cots perambulators nursery furniture and playthings and other accessories there are over five hundred today The market in baby goods is one of the nearest things to a *single-class market* that this country has An expensive perambulator will sell as readily in the East End as in the West End Parents of the nineteen thirties could often afford only a [illegible] for £3 or so today they spend an average of about [illegible] pram and its accessories [11]

*An open question.*—The notions of "similarity" d "equality" of decline have been much used in the going discussion of mortality trends The third line speculation emphasises this similarity of experience various groups If the processes considered above are rating (and they probably are although how importly and in what combination it is not yet advisable guess) the *constant* relationship between classes and upation groups still remains to be explained All e processes may be cancelling each other out but would be truly astonishing if they have happened to ance so nicely It might, perhaps be accepted that y have done so in the five social classes The present r however shows that the infant-mortality rates in rent occupation groups have declined with the same h equality over the forty years; and that this is for both neonatal and the post neonatal mortality with their different immediate and underlying es. The decline in the stillbirth rate has also been ly equal in the five classes so far as the records show—ely since 1939 The parallelism was unaffected by therapeutic revolution of recent years, and applies lly before and after it It has been shown more that the decline has been similar in different parts e country and whether the parents lived in the large res of population in smaller towns or in rural [illegible]

o invoke a "balancing out" argument (such as was ured for the second "speculation") to account for this seems to be postulating too much It is still ceivable that the "lag" in the impact of social changes the infant mortality rates can largely explain the allelism of decline but if so it must be a long lag—er than has hitherto been thought and other factors n are usually considered are surely involved

The theoretical possibility should, however be raised t none of the foregoing suggested explanations will ce—that the mortality rates of the various social ps maintain their relative positions for some reasons et unexplained It is possible that the social levelling the scientific advances of the past half century have rely affected the underlying reasons for the differences een the mortality rates of the class and occupation ps In other words the basic causes of the differes are distinct from the causes of the decline If is so what are the underlying reasons for the social rences in infant mortality? The environmental ons are clearly more than simply physical and omic Perhaps differences in "maternal capacity"[30] possible part of the explanation: that is to say that ch risks are lower medical knowledge greater and universally better there will be differences between ability of mothers to protect their children; and e differences may in turn be related to the social ups which have been studied The emergent principle modern public health[27 31]—that individual behaviour and personal responsibility are becoming crucial to further advance—may thus apply to the field of infant mortality in terms of maternal care Nor should the possibility be ignored that genetic factors may be important—though it is increasingly difficult to maintain this about the present problem Meanwhile miners and clerks—their experience since 1911 and their contemporary record—provide an "experiment of opportunity" wherein much that is important in today's infant mortality might profitably be sought

## Summary

The neonatal (first four weeks) and post neonatal (remainder of the first year) mortality rates for legitimate children of men in various occupation groups—professional workers, farmers teachers clerks textile workers, miners, farm workers and building labourers—are presented for the five periods 1911, 1921 1930–32, 1939 and 1949–50 in England and Wales Mortality rates have declined remarkably uniformly since 1911 and by approximately the same proportion in each occupation group These findings are compared with similar observations that have been made relating to the five "social classes" Such results were unexpected; and three lines of speculation about them are put forward:

(1) There is a time lag in the expression of social improvements in improved health

(2) The composition of social groups is not static and this may affect their mortality rates.

(3) The reasons for the persisting social differences in mortality are in fact imperfectly understood

Some of these questions will be considered in other papers

We are grateful to the staff of the General Register Office for professional technical and computing help; to friends and colleagues for criticism and advice; and to the staff of the Social Medicine Research Unit for much work, in particular to Mrs. I R Murray (secretary) and Mrs V P Hall (computer)

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# Public Health

## ANTHRAX AND BONE-MEAL FERTILISER

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Davies and Harvey (1953) described thirteen cases of malignant pustule in factory workers who handled sun-dried bones imported from the Far East, and a further case in a lorry driver who took away from the factory empty sacks which had contained such bones They were of the opinion that, in Wales, most cases of anthrax in man could be traced to infected sun-dried bones imported from the Far East

Our experience confirms that of Davies and Harvey since 1952 six patients with cutaneous anthrax have been admitted to King's Cross Hospital, five of them from the County of Angus and one from Dundee, in each case there was evidence that the source of infection might have been infected bone meal

### Case-reports

**Case 1** —A man employed on a farm as a tractor driver developed a typical anthrax lesion involving most of his right cheek He was treated with sulphadiazine, penicillin, streptomycin, and anti anthrax serum He made a good recovery with minimal scarring Investigation of the source of infection revealed that he had sustained a minor injury to his face five days previously while treating a grass field with bone meal fertiliser

Shortly after he had become infected a sheep and a bullock died of anthrax on the same farm

**Case 2** —A farm labourer was admitted to hospital very seriously ill with a small anthrax lesion of his neck, very gross œdema, and toxicity A petechial rash was present over the upper part of his chest He died despite intensive treatment with streptomycin, penicillin, and chloramphenicol He was also given anti anthrax serum in an effort to control toxæmia Seven days before his illness he had been engaged in treating fields with bone meal

**Case 3** —A nurseryman had a small typical anthrax lesion of his neck, with moderate œdema but only slight constitutional upset He made a good recovery after treatment with combined penicillin and streptomycin Before his illness he had been spreading bone meal as a fertiliser for plants and shrubs

**Case 4** —A Dundee dock labourer had a malignant pustule on his forehead, with considerable œdema of his face and neck He was severely toxic Treated with combined penicillin and streptomycin he made an excellent recovery Five days before his illness he had been unloading a cargo of crude bone meal He did not actually handle the bags, but there was a good deal of "bone meal dust" around in the process of unloading

**Case 5** —An agricultural worker had a lesion typical of anthrax on his neck, with moderate surrounding œdema, accompanied by considerable constitutional upset He made a good recovery after treatment with combined penicillin and streptomycin He had been spraying bone meal fertiliser about a week before his illness

**Case 6** —A mechanic's labourer, who had no agricultural connection other than working in his own garden, developed an anthrax lesion on his right forearm, with surrounding œdema but very little general upset Combined penicilli and streptomycin was effective in clearing the lesion Immedi ately before his illness he had been handling bone-meal as fertiliser in his garden

### Bacteriological Findings

The laboratory investigation of the patients consist in examination of smears for the presence of organis morphologically resembling *Bacillus anthracis*, and culture of swabs taken from the lesions

RELATIONSHIP OF BACILLI ON MICROSCOPY AND CULTU

| Case no | Bacilli in smears | Culture |
|---|---|---|
| 1 | + | + |
| 2 | + | + |
| 3 | ? | − |
| 4 | + | + |
| 5 | + | + |
| 6 | + | − |

In the present six cases we demonstrated organis morphologically resembling *B anthracis* in smears in fi and isolated *B anthracis* in four (see table)

In case 3 on microscopy a few "ghost like" bac were seen which stained very poorly with methylene bl and Giemsa and were gram negative

The four strains isolated gave typical colonial a morphological appearances and were pathogenic for m and guineapigs, giving the typical post mortem app ance in these animals

The sensitivity of the strains was tested in vitro by plate technique using Evans's sensitivity discs, and the strains were sensitive to penicillin, streptomy chloramphenicol, aureomycin, and oxytetracycline

*Bone meal* —Samples of bone meal handled by ca 2–6 were obtained, but we were unable to isolate, demonstrate by other methods, *B anthracis* from the Dr A J H Tomlinson, however, isolated *B anthra* from the bone meal associated with cases 3–5 In cases 3, and 5 the bone meal came from the same commerc batch, and the time of occurrence of the cases extend over two years

### Discussion

Bacteriological proof that the infection came fro handling bone meal was obtained in three of the prese cases, and presumably it arose in the same way in th remaining three cases In the case of the dock labour the bone meal was in crude form, but in the five oth cases it was refined It therefore seems that either th refined product had not been subjected to any proc intended to sterilise it, or such a process had be inadequate to destroy the spores

In January, 1953, the Minister of Agriculture stat in reply to a question in the House, that "there was li doubt that imported animal products, such as bone mea

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38 Morris, J N (1947) *Lancet* ii 341
39 — (1951) *Brit med J* ii, 648
40 — (1953) Paper given before British Sociological Association s Conference on Social Policy and Social Sciences Table IX.
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44 Orr J B (1936) Food, Health and Income London
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48 — (1923) Census of England and Wales 1911 vol XIII Fertility of Marriage part II
49 — (1927) Decennial Supplement England and Wales 1921 Part II Occupational Mortality Fertility and Infant Mortality
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were a fairly common source of (anthrax) infection As a first step the Ministry of Agriculture was now discussing with the appropriate trade associations further measures to reduce the risk from this source' (see *Lancet* 1953)

Bone-meal appears to be used extensively as a fertiliser not only by the agricultural community but also by a wide section of town dwellers in their gardens. It is obviously desirable to ensure that bone meal used in this country should be rendered safe from the hazards of anthrax

## Summary

Six cases of anthrax occurring in Dundee and district are described

These cases occurred over a period of two years (1952–54)

Imported bone-meal from the Far East was the source of infection in three cases and probably also in the other three.

We wish to thank Prof W J Tulloch for his interest and advice; Dr J M. Thomson medical officer of health County of Angus, and Dr E H. Weir Duncan medical officer of health, Greenock, for samples of bone meal and Dr Tom son, of the Public Health Laboratory Service for isolating *B. anthracis* from samples of the bone-meal associated with cases 3–5 and for allowing us to cite his findings.

REFERENCES

Davies D G Harvey R W S (1953) *Lancet* ii 880
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## Diphtheria since 1945

In support of its diphtheria prophylaxis campaign the Ministry of Health has issued the following figures for diphtheria notifications and deaths in England and Wales over the past 10 years[1]:

| Year | *Deaths* | *Notifications* |
|---|---|---|
| 1945 | 722 | 18,596 |
| 1946 | 472 | 11,986 |
| 1947 | 244 | 5609 |
| 1948 | 156 | 3575 |
| 1949 | 84 | 1890 |
| 1950 | 49 | 962 |
| 1951 | 33 | 664 |
| 1952 | 32 | 376 |
| 1953 | 23 | 266 |
| 1954 | 9 | 182 |

The deaths include late effects—i.e. those taking place more than a year after the acute episode Figures for 1954 are provisional

The object of the campaign is to secure immunisation of at least 75% of babies in the first year of life The proportions immunised were 28% in 1951, 31% in 1952, 30 4% in 1953 and 35 75% in the first half of 1954

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[1] Ministry of Health Circular no. 5/55

## Infectious Diseases in England and Wales

| Disease | Week ended February | | | |
|---|---|---|---|---|
| | 5 | 12 | 19 | 26 |
| Diphtheria | 16 | 14 | 16 | 13 |
| Dysentery | 979 | 1110 | 1145 | 1[illegible]37 |
| Encephalitis : | | | | |
| Infective | 1 | 2 | 2 | 1 |
| Postinfectious | 1 | | 1 | 1 |
| Food-poisoning | 137 | 94 | 112 | 125 |
| Measles excluding rubella | 12,[illegible]20 | 18 30[illegible] | 19 978 | 23 700 |
| Meningococcal infection | 43 | 24 | 43 | [illegible]4 |
| Ophthalmia neonatorum | 30 | 30 | 48 | 32 |
| Paratyphoid fever | 7 | 4 | 3 | 3 |
| Pneumonia primary or influenzal | 1157 | 1156 | 10[illegible]1 | 924 |
| Poliomyelitis : | | | | |
| Paralytic | 9 | 0 | 13 | 9 |
| Non-paralytic | 4 | 7 | 8 | 1 |
| Puerperal pyrexia | 210 | 251 | 213 | 220 |
| Scarlet fever | 701 | 716 | 683 | 675 |
| Smallpox | | | | |
| Tuberculosis : | | | | |
| Respiratory | 751 | 767 | 713 | 76[illegible] |
| Meninges and C.N.S. | 13 | 1[illegible] | 13 | 20 |
| Other | 96 | 73 | 101 | 87 |
| Typhoid fever | 8 | 1 | 4 | 4 |
| Whooping-cough | 2213 | 2005 | 1910 | 1678 |

Not including late returns

# In England Now

## *A Running Commentary by Peripatetic Correspondents*

DESPITE our personal dollar problem we hadn't been in the States for more than a few days when we realised that we had to have a car I wasn't seriously concerned when my wife remarked upon the difficulty of transporting the week's provisions as well as the children up the hill from the supermarket After all, shopping and care of the children are a woman's tasks Or so I thought until we saw Dr H. from downstairs returning home laden on a Friday evening It was after my first journey home, with two enormous brown paper bags full of groceries, that I made my decision Surely I argued a man in my position, and with my professional responsibilities, needed a car It was just after Christmas when I began the rounds of the used-car lots. Curiously my rapport with the dealers always deteriorated when they learned how much I had to spend—but then I came to Bill Bill was a Canadian and a sort of Commonwealth solidarity made us pals from the start. He it was who introduced me to Josephine, as she was later christened by the children. She was then just a dark green coupé, in need of a coat of paint, standing forlornly in the lot. A 1941 model with 80,000 miles to her credit, she was a vintage specimen by American standards but as I examined the independent front suspension, fluid drive, steering wheel gear-change radio, and heater, I could feel myself weakening particularly when she started at a touch. 'She's yours for a hundred bucks' said Bill, and in no time I was writing out the cheque. I was only slightly chastened when I discovered that the insurance would cost more than the car

It was New Year's Day, one of those glorious crisp and sunny New England days, when I brought Josephine home to meet the family 'You can even lock the doors,' I pointed out, turning the key I must say Bill was very good he was up within half an hour with a new ignition key, and soon extracted the broken fragment from the lock Next day we drove to hospital, I didn't notice the snow till it was time to go home and by then poor Josephine was submerged Laboriously I uncovered her and climbed in; but the battery was dead and I went home by bus For several days she lay there until the thaw came and Pete from the garage next door came round and gave her a push At once she started and we were on our way; we hadn't gone more than half a mile when the engine stalled In the din of the traffic flashing by on either side, Josephine lay silent, unperturbed and unresponsive while the cacophony of impatient horns in the cars behind mounted in intensity At long last the Buick in the rear nosed its bumper up to mine gently accelerated and she came to life again Four times more on the journey she stalled and when finally I reached Bill's garage I was prepared to admit that being a car-owner was quite a responsibility

Space will not permit me to detail her many later frivolities, such as the occasion when she ran off down the drive by herself, or her many electrical failures invariably solved by a smart blow with a hammer on the battery connections; and, though we secretly felt it to be over-indulgence we never divulged to her our feeling that no real lady should require four quarts of oil each week. But when we came to understand her better and to indulge her minor fancies she never failed us.

When the time came to return home the parting was a sad one for we were losing a member of the family Now we have a new car and the children have tried to christen her Betsy but she has so little character that it hasn't caught on certainly there can never be another Josephine.

* * *

Amateurs of hydriotaphia can find few pleasanter spots in which to hydriotaphe than the British Cemetery, Funchal. Quiet and secluded behind high walls under the old Fort cypress bowered and decked—in February—with mimosa sprawling scarlet geraniums iris, and violets, its urns and tablets reflect the changing patterns of mortality The earliest date we found was 1809 The British occupied Madeira from 1807 to 1812 and the tablet commemorates Emma Frances, the wife of Lieut Colonel Peachy

# Public Health

## ANTHRAX AND BONE-MEAL FERTILISER

W M JAMIESON
M.D St And, D P H
PHYSICIAN SUPERINTENDENT,
KING'S CROSS HOSPITAL,
DUNDEE

D M GREEN
M B St And
LECTURER IN BACTERIOLOGY,
UNIVERSITY OF
ST ANDREWS

Davies and Harvey (1953) described thirteen cases of malignant pustule in factory workers who handled sun-dried bones imported from the Far East, and a further case in a lorry driver who took away from the factory empty sacks which had contained such bones They were of the opinion that, in Wales, most cases of anthrax in man could be traced to infected sun-dried bones imported from the Far East

Our experience confirms that of Davies and Harvey since 1952 six patients with cutaneous anthrax have been admitted to King's Cross Hospital, five of them from the County of Angus and one from Dundee, in each case there was evidence that the source of infection might have been infected bone-meal

### Case-reports

**Case 1** —A man employed on a farm as a tractor driver developed a typical anthrax lesion involving most of his right cheek He was treated with sulphadiazine, penicillin, streptomycin, and anti anthrax serum He made a good recovery with minimal scarring Investigation of the source of infection revealed that he had sustained a minor injury to his face five days previously while treating a grass field with bone meal fertiliser

Shortly after he had become infected a sheep and a bullock died of anthrax on the same farm

**Case 2** —A farm labourer was admitted to hospital very seriously ill with a small anthrax lesion of his neck, very gross œdema, and toxicity A petechial rash was present over the upper part of his chest He died despite intensive treatment with streptomycin, penicillin, and chloramphenicol He was also given anti anthrax serum in an effort to control toxæmia Seven days before his illness he had been engaged in treating fields with bone meal

**Case 3** —A nurseryman had a small typical anthrax lesion of his neck, with moderate œdema but only slight constitutional upset He made a good recovery after treatment with combined penicillin and streptomycin Before his illness he had been spreading bone meal as a fertiliser for plants and shrubs

**Case 4** —A Dundee dock labourer had a malignant pustule on his forehead, with considerable œdema of his face and neck He was severely toxic Treated with combined penicillin and streptomycin he made an excellent recovery Five days before his illness he had been unloading a cargo of crude bone meal He did not actually handle the bags, but there was a good deal of "bone meal dust" around in the process of unloading

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### Bacteriological Findings

The laboratory investigation of the patients consisted in examination of smears for the presence of organis morphologically resembling *Bacillus anthracis*, and culture of swabs taken from the lesions

RELATIONSHIP OF BACILLI ON MICROSCOPY AND CULTU

| Case no | Bacilli in smears | Culture |
|---|---|---|
| 1 | + | + |
| 2 | + | + |
| 3 | ± | – |
| 4 | + | + |
| 5 | + | + |
| 6 | + | – |

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62 Taylor I (1954) *Lancet*, i 202
63 Thompson B (1954) *Med Offr* 91 235
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| Disease | Week ended February | | | |
|---|---|---|---|---|
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| Diphtheria | 16 | 14 | 16 | 13 |
| Dysentery | 970 | 1110 | 1145 | 1237 |
| Encephalitis: | | | | |
| Infective | 1 | 2 | 2 | 1 |
| Postinfectious | 1 | | 1 | 1 |
| Food-poisoning | 137 | 94 | 112 | 125 |
| Measles, excluding rubella | 12 720 | 18,307 | 19 078 | 23 709 |
| Meningococcal infection | 13 | 24 | 43 | 21 |
| Ophthalmia neonatorum | 39 | 30 | 48 | 32 |
| Paratyphoid fever | 7 | 4 | 3 | 3 |
| Pneumonia, primary or influenzal | 1157 | 1150 | 1021 | 921 |
| Poliomyelitis: | | | | |
| Paralytic | 0 | 9 | 13 | 9 |
| Non-paralytic | 4 | 7 | 8 | 1 |
| Puerperal pyrexia | 240 | 231 | 213 | 220 |
| Scarlet fever | 791 | 746 | 682 | 675 |
| Smallpox | | | | |
| Tuberculosis: | | | | |
| Respiratory | 781 | 707 | 713 | 762 |
| Meninges and C.N.S. | 13 | 12 | 15 | 20 |
| [illegible] | 96 | 3 | 101 | 87 |
| Typhoid fever | 6 | 1 | 4 | 1 |
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# In England Now

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> "C McD (*sic*) gave early indications of a decided piety and, when cut off by a pulmonary ailment, as mourning survivors are tempted to think too soon for them, though seasonably for her "

In a third group, beginning about the turn of the century, the age-incidence suddenly shifts into the seventies and eighties, with the advent of the wealthy English invalids and *malades imaginaires* whose lives the warm winter sun of this island paradise successfully prolonged We found a grim reminder of a disease which has quite changed its character—and may do so again—in a tablet to "James, Charles and Robert Payne, who died at the early ages of 5 years, 3 years and 18 months" in June, 1857, of scarlet fever Incidentally, the lettering of the pre-1850 tablets, presumably done on the island, showed a simplicity and beauty reminiscent of Eric Gill himself

And who, who was "George Pepple, King of Bonny, died Nov 1st 1888 R I P"?

* * *

The Regency period saw the Industrial Revolution, and the breaking up of machinery by the Luddites But, though the central theme in the décor at the Ideal Home Exhibition is the Regency period, it is unlikely that the army of housewives streaming to Olympia are bent on rebellious violence Here they can study all the latest machines designed to ease the housework, electric polishers, washing machines, automatic wringers, and electric mixers can all be seen in action For those without electricity, or who need help at a more modest price, there are new types of dusters and floor brushes with two revolving circular heads The main hall is filled with furniture, the modern style being particularly prominent, and with cooking and the larger electric appliances, also on the ground floor are the Nylon Fair (limited, rather disappointingly, to stockings on false legs), the toy section, dominated by the painting-by-numbers sets, and the modern houses built together as the Houses on the Hill On the first gallery are the stalls of household gadgets and the Food Fair, as always offering many little snacks Also on this floor, in one corner, there is *Family Doctor* Street, with the *Family Doctor* grocery shop and the *Family Doctor* drapers, selling ordinary branded articles The caravans, a R A F bungalow married quarter at present being built in Cyprus, and the do-it-yourself exhibition are on the second floor Downstairs again the gardens are a retreat from bleakness and snow outside Among the flower gardens is a vegetable garden with much produce growing succulently At the entrance to the gardens are stalls that show that not only housework is becoming mechanised Besides small ploughs and rotary hoes you can now buy some of your seeds already sown Indeed, if the Regency was the era of the Industrial Revolution, today is the era of the Domestic Revolution

* * *

I am no stickler for priorities, but I really don't see why your young contributor's examiner, even though "an eminent physician by all standards," should get away with the credit for suggesting a method using Benedict's reagent which would "save the country £50,000 a year' If your contributor turns to p 282 of the ninth edition of Joslin's *Diabetic Manual* (1953) he will find that this shrewd Grand Old Man of diabetes had already thought of it

> "Four drops of the urine to be examined are placed in a test tube and to this are added 2 5 cc (an ordinary teaspoon holds about 5 cc ) of Benedict s solution The test as originally described was performed by using 8 drops of urine and a trifle more than a teaspoonful of Benedict s solution, but if the smaller quantity is employed universally by diabetics I once reckoned it would amount to a saving of more than $1 [illegible] 000 a year What a sum to apply for the study and care [illegible] with diabetes!

# Letters to the Editor

## AFTER THE ACCIDENT

SIR,—Commenting, on Feb 5, on the Sutton Coldfield railway accident you spoke of the need of "detailed preparedness" for the evacuation of casualties after any disaster But what is equally necessary, and much harder to achieve, is "detailed preparedness" at all times for the *treatment* of the severely injured, whether they come in large numbers or singly

We now know that, even with severe multiple injuries, life can often be saved by early transfusion—but only if surgery follows quickly and at the right time We know that surgery is most effective when the blood volume has been restored to normal, and that this often requires very large transfusions [1] And we know that the long "illness of trauma" can be prevented only by early restoration of blood volume, by early surgery aimed both at repair and at the prevention of infection and by the very careful postoperative treatment lasting many days Yet many people remain reluctant to accept the plain fact that this kind of skilled treatment, at th right time, can be provided only by hospitals normally staffed and geared to the handling of such emergencies.

After any serious accident, the chief need is to get th injured people quickly under the care of surgeo experienced in the clinical diagnosis and assessment severe injury, and, since the rescue and ambulan services complete their task with remarkable rapidity it would seem wise to continue to lay emphasis "speed of evacuation" to prearranged hospitals is these hospitals that have to be kept in a state "detailed preparedness" to treat casualties, eith single or numerous

After the Sutton Coldfield accident the whole time st of the Birmingham Accident Hospital were very quick mustered Those off duty quickly returned and were ful prepared, with all facilities at hand, when the first serio casualty arrived, after a ten mile journey, just 45 minut after the crash

Should the numbers of very severely injured pro too heavy for one hospital, then the first 50, say, cou be received by that hospital, giving time for a seco hospital to collect its staff and prepare for the ne wave of casualties Two such hospitals could take the f initial responsibility for the casualties from almost peace-time disaster

An essential part of the mass casualty scheme agreed Birmingham is the forwarding of precise information to t medical officer at control headquarters In so far as t concerns the treatment of the seriously injured, he require know the numbers of the injured and their needs After accident such as the one at Sutton, this information may be available for some time Very precise information o however, be given by "receiving" hospitals on such import matters as the need for more help from the regional blo transfusion service, or the need to alert further surgical tea at other hospitals for reparative surgery if this load becom too heavy When necessary, patients can be sent on to th other hospitals with a reasonable diagnosis and with all t benefits of full medical first aid

Unfortunately, such well equipped and well staff accident hospitals and accident departments as we ha in Birmingham are to be found in few places But th are an essential part of "detailed preparedness" the treatment of severe injury, and mass disaster does more than spotlight the need for them The ann national casualty list from accident (10,000 killed, o 200,000 seriously injured, and over 1,250,000 requiri hospital treatment) underlines this everyday need

The Ministry of Health, however, believes th to initiate any change of policy in this matter, the

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1 Ruscoe Clarke Topley E, Flear, C T G *Lancet*, 1955 (in t press)

be a solid weight of clinical opinion in its favour neither clinicians nor administrators are widely strongly interested in the development of an efficient lent service In direct evidence of this is the fact in the 14 years of the Birmingham Accident Hos "experiment," we have lost many of our well ed and experienced staff—not because the technical human challenge of the work is unattractive but use more favourable and less exacting conditions been offered elsewhere

a long view is to be taken we must consider not the detailed planning and strategic siting of large dent departments attached to general and teaching itals, but also the terms of training and service of personnel—at all levels—needed to staff such emer cy services over the 24 hours of each day Since the isation must always be fully prepared it cannot heavily populated areas be a "part time" service minor responsibility

ur rescue and ambulance services already function h commendable efficiency, and the most seriously ured, if evacuated quickly, travel ten miles and more mparatively safely even with our present design of bulance With better ambulances the "safe" distance ght well extend to twenty five or thirty miles In a all country like ours the strategic siting of fully uipped and staffed accident services each attached to large general hospital would go a long way to ensure per medical care for all the many people who are iously injured on road or railway at work or in the me

irmingham Accident Hospital
Birmingham, 15

WILLIAM GISSANE

## HOSPITAL STAFFS

ir,—I was very interested in the tables issued by the stry of Health on the consultant and senior registrar ablishment[1] Clearly little increase is likely in the sultant establishment as will be seen from table which gives the numbers of consultants in each specialty m Dec 31 1952 to June 30 1954, the increase in the mbers of consultants in general medicine general gery and obstetrics and gynaecology was 12 0 and spectively Most of the other specialties show very le increase during this period. The present figures refore seem to be stable

I am surprised to see that the retiring age of 65 is not enforced since there are so many senior registrars ouring for posts In the three major specialties re the congestion is greatest there were 23 physicians urgeons, and 11 gynaecologists over 65 (born in 1889 earlier) who had not retired when this table was piled. Though it is quite possible that each of these only have a few sessions, their retirement would e at least some vacancies As there is to be no further tant expansion of the consultant services it seems ulous that fully trained senior registrars are being n prevented from obtaining these retirement vacancies ow virtually their only hope of promotion Before health service most hospital boards made 60 the ing age

n table III (senior registrars in each specialty) taking eral medicine only there are 22 senior registrars in r fourth year and 77 "others"—which presumably es men in their fifth and subsequent years—making tal of 99 In other words there are 99 candidates ing posts which will become or should become vacant ugh retirement According to table I there should 13 in 1955 18 in 1956 and 11 in 1957 but as each ntment may only represent a few sessions the number tual appointments will be less than this probably average of about 10 a year Senior registrars in their th and subsequent years therefore only have about 10 chance of a consultant vacancy in their specialty

Something *must* be done for these men, who are fully trained and presumably are fully competent since otherwise they would not have reached and retained their present status I hope that the new committee set up by the Ministry of Health will consider what practical steps can be taken to help them

Mayday Hospital
Thornton Heath
Surrey

G P BAKER

SIR —The "break down" of figures for consultant staffs published by the Ministry of Health, reveals strikingly uneven expansion

Numerically approximately equal groups are made up by (A) major specialties (general medicine general surgery, obstetrics and gynæcology [2106 in 1949]) and (B) specialties in which full clinical responsibility is the exception (mental health, radiology radiotherapy physical medicine pathology anæsthesia [1001 in 1949]) The expansion in the number of consultants and the present numbers of senior registrars are as follows

|  | *Expansion since 1949 (%)* | *Present no of senior registrars* |
|---|---|---|
| Group A | 13 | 510 |
| Group B | 36 | 289 |
| All specialties | 25 | — |

These figures do not take account of the further surplus in group A of potential specialists holding university and other appointments

It may be argued that it was in the non-clinical specialties that the need for expansion was greatest But clearly the present numbers of senior registrars in group A represent highly trained man power required to meet definite clinical needs and not merely "trainees" retained for future needs It follows that real levelling up of expansion is needed in those general categories which have been and always must be, the basis of a hospital service

SENIOR REGISTRAR

SIR,—Not every good man is fortunate enough to come along at the right time for a registrar vacancy in a teaching hospital

For several years after the beginning of the health service many men as good as those who obtained registrar appointments in teaching hospitals went into the regional hospitals The experience and training these men have obtained in many of the large regional hospitals have been as good as are obtained in the teaching hospitals

When it comes to a consultant appointment however the regional man very frequently comes up against an attitude of mind which immediately places him in an inferior position Most of these men never even reach the short list to get a hearing There is in the hospital service today one way traffic through the teaching hospitals to most senior appointments particularly in the three main specialties, in all hospitals The interchange system for senior registrars was brought in with the main intention of trying to right this situation and give some incentive for men to take house-officer and registrar posts in regional hospitals With few exceptions this intention has been frustrated by the one way traffic system at this level

For nigh on two years now the profession has been deliberating how to staff the regional hospitals. The creation of a new type of post in regional hospitals passage through which will be the normal way to consultant posts will do nothing to staff regional hospitals when one way traffic is in operation

Honourable men have laboured with good intent to try to find a solution to this problem, but within constraints which make the problem insoluble These constraints are mainly attitudes of mind which stem from the past but are not applicable to the present or the future

REGISTRAR

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1. See *Lancet*, Feb 26 1955 p 418

## HEALTH EDUCATION

SIR,—Health education in this country has always been viewed with mixed feelings by our profession The reasons are many, and justifiable Perhaps the two most important are that medicine, even today, is still as much an art as a science, and if no two doctors can always agree in detail about the care of one patient, how can they agree in principle about the conduct of an incompletely delineated condition ? For Dr A to talk in simple terms of a disease complex in the abstract, and then Dr B's patient to tell him just how he should be treated (according to Dr A) is awkward Secondly, there exists the genuine feeling that, in describing the details of signs and symptoms of a disease and then its treatment, we may be telling a neurasthenic enough for him to confuse us, and initiate him into the realms of Munchausen's disease "Ignorance is bliss" and "A little knowledge is a dangerous thing" are both quoted to support these points of view

Against this the educationists say that a neurasthenic will be just as neurasthenic when he is ignorant as when he is informed, until his fears are completely resolved —and these fears mostly rest on ignorance The trouble, they say, lies not in education, but in incomplete education "Trust your doctor, he knows best what is good for you" may be excellent therapy for some types of elderly spinster, but does it achieve its purpose for all ? We live in a technological age, and the doctor can safely discard his display of witchcraft and admit he is a scientist in some circles Explanations of just what he is doing, and why, will often reassure patients and their families if supplied within the framework of their understanding—"kitchen similes" are valuable in many homes, and quite detailed explanations are appreciated in others But these explanations take time, and so health education in the mass must replace, to some extent, the personal explanation

Here television has an immense part to play, for to the immediacy of real live speakers is added the intimacy of the home circle viewing the complicated demonstrations in the studio which may have taken weeks to assemble The size of the audience, and the fact that they all view the programme simultaneously and discuss it in unison next day, adds further to the short term impact Yet your reference (Jan 29, p 247) to the W H O memorandum makes no mention of this new medium for education

The twelve programmes which I arranged for the B B C two years ago revealed conclusively that difficult and advanced concepts could be accepted and understood by a large audience when presented sincerely and clearly, and their message appreciated even by sufferers from those diseases

Two examples come vividly to mind One was an elderly man in hospital with a recurrent peptic ulcer who had just had a severe hæmorrhage His surgeon was discussing his condition with him, leading up to breaking to him gently the advice that he have a partial gastrectomy Quite soon the patient said, "I know what you are going to say, Doctor, you want to cut out part of my stomach—I was wondering when you were going to Go ahead" He was perfectly cheerful and assured—he knew the facts

The second example was an elderly hyperpietic who was reluctant to have E C G electrodes fitted to his arm His wife said, "Don't be silly Tom, it's only that machine you saw on T V last week", and he was immediately reassured

In that series I took special care to present only conditions for which a positive cure was known, or a hopeful outlook could be assured Perhaps the time is now ripe for a further series in which some genuine difficulties which face the profession can be explained, and the different lines along which research is progressing sh

A large new field of public education is now opening before us, whether we like it or not The manufacturers of patent medicine have not always presented medicine impartially and accurately in their advertisements—particularly of the strip cartoon type—and we do not want to see comparable vignettes enacted under the ægis of the I T A On the other hand, other manufacturers have presented valuable factual teaching, particularly to our profession, and an extension of that practice could be of immense benefit to patients and practitioners alike But in these programmes, whether for the B B C, or I T A, we must maintain our sincerity and honesty, and refrain from sensational journalese if we are to keep faith with our colleagues and our patients

London, W 1 BRIAN STANFORD

## LIFE-ASSURANCE UNDERWRITING

SIR,—Dr Khambatta's letter of Feb 26 gives an entirely wrong impression There are, as he says, two accepted methods of imposing special terms for life assurance—by charging an extra premium or by imposing a debt which may be either constant or diminishing The numerical system, which is based on a series of plus and minus ratings for tabulated good and bad points only indicates the amount of the excess mortality if any It is therefore not an alternative method of treating extra risks but an alternative to the traditional method of underwriting by the Chief Medical Officer and the Actuary The numerical method is in general use by American and Canadian companies, and I believe that well over 90% of cases can be accepted without submission to those responsible for underwriting Even so the cases which fall outside certain limits of excess mortality have to be assessed individually

I think it is probable that recent advances in medicine are far more likely to be brought into account under the traditional method than the numerical method Surely anybody responsible for fixing a definite number to represent an excess mortality is likely to wait until he has some statistical evidence to support it On the other hand the Medical Officer assessing a case on his own judgment can say at an earlier stage that the new methods of treating this disease are so effective that the case can be accepted at ordinary rates

Enlightened Medical Officers were accepting a non-tuberculous spontaneous pneumothorax at ordinary rates 20 years ago, purely on their own judgment Lenient decisions in this and similar cases have no relation to any mystical powers inherent in the numerical rating system

Medical Sickness Annuity and Life
Assurance Society Ltd.,
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London, W 1

E A J HEATH
Manager and Actuary

## COLD BATHS

SIR,—I am delighted that at last some doubts have arisen about the wisdom of compelling school children to take a cold bath every morning

If school mastering is, as Ian Hay put it, "driving a herd of unwilling donkeys up the slopes of Parnassus," the addition of cold water makes it more like a perpetual sheep-dipping The value of such a practice seems slight, and I for one see no virtue in the faint hearted alternative Mr Vincent suggested in his letter last week—namely, lowering the bathroom temperature There are far too many sepulchral bathrooms as it is, without school fees being charged to maintain conditions which would not be tolerated in a second rate boarding house In a first rate boarding school, however, the cold bath may satisfy both masters and pupils, as it provides the maximum of discomfort to the recipient, while assuring him the minimum of cleanliness

Shaw observed that the English frequently believe themselves to be moral when in fact they are only uncomfortable Few of us have the sanctity to emulate the Blessed Ethelfleda, Abbess of Romsey, whose practice it was to chant the Psalms while immersed at night in the bed of a running stream. If mortification of the flesh is to benefit the soul (and one doubts whether it has other justification) it should be voluntary and not compulsory

No doubt the shuddering plunge is mitigated for the partan children as they reflect that at the same time he headmaster and his entire staff the matron, and the haplain are lustrating themselves with ice water to ractise what they preach Or are they ?

Middlesex Hospital,
London W 1

J W DICKSON

## TETANUS TREATED WITH INTRAVENOUS MEPHENESIN

SIR,—In his report of a case of tetanus treated with ephenesin (Feb 26) Dr Docherty makes the surprising tement that the drug 'does not act on the higher tres and therefore does not affect consciousness. e dosage used in this case—up to 18 g in twenty four urs—is low and would not be expected to have any ch effect given slowly intravenously, as it was But owsiness is the most commonly reported side effect of phenesin and I have more than once seen complete ough brief loss of consciousness follow rapid intra nous infusion of the pure drug in saline Pronounced owsiness is almost invariable with doses of 2–4 g given travenously in five to fifteen minutes and such doses n be needed in tetanus Mephenesin in large doses is powerful cerebral depressant and sedation with the ual drugs may have to be reduced to avoid over dation when large doses of mephenesin (e.g about g in an hour) are used Commercial liquid preparations o contain alcohol which adds to the sedative effect.

Kew Gardens, Surrey

D R LAURENCE

## MENTAL HEALTH AND PUBLIC HEALTH

SIR,—In an address to a joint meeting of the Scottish anch of the Society of Medical Officers of Health and e Scottish division of the Royal Medico Psychological ociation, Dr MacQueen[1] said

> The Health Visitors—about one for every 2,500 people the best staffed areas and one for every 5 000 in the worst as—are again not experts in psychology they have their eral nursing training, with nowadays a slender intro tion to psychology included a subsequent midwifery ning, and—usually after two or three years as a hospital f nurse and a ward sister—a course of full time study for Health Visitor s Certificate this course lasting at present m six months to one academic year but likely in the near re to become standardised everywhere as an academic r and including some six or seven lectures or lecture onstrations on mental health.

In his letter of Feb 26 he asks whether I am ' aware the very large amount of time devoted in the health itor's training to the psychology of development and ed subjects.

There is no mention of psychology in the syllabus of eral training of the General Nursing Council for land Mental diseases are mentioned : a minimum two hours teaching in the three years of training is ommended I think that this barely a day s work out four to six years' training gives an orientation towards sical illness and away from mental illness which its the health visitor for work in the field of mental lth

On the other hand, our doctors get a much better impression the importance of mental ill health during their course of dy In Edinburgh the medical student is required to nd 40 lectures on psychiatry and psychology and 20 ical demonstrations; and there is an elective clinical k in the wards of the Edinburgh mental hospitals. The graduate students in the D P H and D P H courses get 20 tures and demonstrations on mental health and 20 lectures on psychology This may not reflect adequately the importance of mental ill health as a public health problem, but clearly a person so trained is hardly to be compared with a health visitor

Having said that, let me make suggestions for the improvement of the training of both the general nurse and the health visitor Firstly they should be made aware that a third to a half of all hospital beds are for the mentally ill and that mental and nervous troubles approach this proportion of all ill health There is no better way of doing this than by prescribing a period of training in a mental hospital amounting to not less than six months out of the three years general training The title Registered General Nurse is at present a misleading one Secondly, during her post-registration training the health visitor would greatly benefit by some time spent working with the authorised officer of a local authority and with the psychiatric social worker attached to a hospital or clinic With this additional training the health visitor would be much better qualified to work in the field of mental health

Usher Institute
University of Edinburgh

DONALD CAMERON

## DIET AND ATHEROSCLEROSIS

SIR,—Many of your readers will be familiar with the laboratory and field studies of Professor Keys and his associates[1] bearing on the correlation between fat intake serum-cholesterol concentration and incidence of athero sclerosis which is now the leading cause of death among adults in the United States and possibly in other Western countries[2] Further supporting evidence has been published from this centre[3 4] where we have noted firstly that low serum-cholesterol values are found in the South African Bantu whose fat intake provides little more than a third of the proportion of calories that it does in Americans and secondly, necropsy evidence shows that the severer complications of atherosclerosis are far less common among the Bantu than among comparable American hospital populations

It is thus tempting to assign considerable significance to the level of fat intake in the ætiology of the disease At the same time there are two contradictory items of evidence which cannot be ignored and which caution against attaching too much significance to level of fat intake per se

> Firstly the fat intake of Eskimos is high ; it supplies over 40% of their calories[5] Yet available data (admittedly incom plete) indicate that their serum-cholesterol values are not abnormally elevated moreover cardiovascular disease is almost unknown among these people or for that matter among the inhabitants of the Yukon who also have a high fat consumption[6]
>
> Secondly low serum-cholesterol values are found among strict vegetarians despite their high fat intake in three recent investigations fat supplied 33% 34% and 35% respectively of their calories[7–9] *It is not yet known however whether vegetarians in Western countries suffer less than non vegetarians from severe atherosclerosis.*

Arising from our investigations on the Bantu there is one aspect which impressed us and to which *attention* might be drawn—namely a low fat intake is only one feature of their pattern of diet furthermore a *low* incidence of atherosclerosis is but one feature of their disease pattern The Bantu diet while probably adequate in calories and gross protein, is low in animal protein fat cholesterol sugar certain mineral salts and vitamins, yet high in carbohydrate and crude fibre Among these people there is a high incidence of liver disease, though a low incidence not only of atherosclerosis, but of appendicitis, eclampsia, peptic ulcer, diabetes, gallstones, urinary stones, and certain forms of cancer To what extent pattern of diet, with its concomitant pattern of metabolism, influences the incidence of the diseases mentioned, still requires considerable investigation But one wonders whether levels of fat intake and of serum-cholesterol must be *within* a certain dietary setting before they are of significance in regard to atherosclerosis In other words, is one justified in being too hopeful that reduction of fat intake only in the diet of middle class Western population groups will markedly retard or arrest the development of the disease ?

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[1] MacQueen, I A G *Publ Hlth Lond* 1954 68 21

[1] Keys A *Voeding* 1952, 13 539
[2] Morrison, L M *Ann. intern Med* 1952 37 1172.
[3] Walker A R P, Arvidsson U B *J clin Invest.* 1954 33 1358
[4] Higginson J., Pepler W J *Ibid* p. 1366.
[5] Sinclair H M. *Proc Nutr Soc.* 1953 12 69
[6] Duncan, G C *Lancet* 1947 ii 919
[7] Groen, J Tjiong B K Kamminga C E., Willebrands A F *Voeding* 1952 13 556
[8] Donath, W F., Fischer J A Iyebergen, H C M., Wijn J F *Ibid* 1953 14 153
[9] Hardinge M G., Stare F J *Amer J clin Nutr* 1954 2 83

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A R P WALKER

## CYTOTOXIC AGENTS IN MALIGNANT DISEASE

SIR,—In your leading article of Feb 26 you state " Blackburn and King [1] had no success from administration of tretamine to 4 patients with reticulosarcoma " Actually 2 of the 4 cases of reticulosarcoma responded satisfactorily to the first course of T E M for periods of four and sixteen weeks

Royal Infirmary, Sheffield

~~E K BLACKBURN~~
G M KING

## PSYCHOLOGICAL ASPECTS OF UTERINE DYSFUNCTION

SIR,—The letter from Dr Tylden and her colleagues (Feb 19) contains several points upon which I wish to comment

They feel that both their own work in 1950 and my recent paper should be considered as preliminary studies, apparently disregarding the fact that I only claimed mine to be " a pilot investigation "

Much of their criticism seems to stem from a misconception of my clearly defined field of study and the nature of uterine dysfunction, which was described as early as the third paragraph of the paper The dysfunction group were " those cases of vertex presentation where (in primigravidæ) prolongation of labour beyond twenty four hours, or difficulty in labour, was judged to be due *solely* to inadequate forces or to resistance of soft tissues " It is therefore surely implicit that there were no other obstetric abnormalities, and operative interference was due entirely to the character of labour The fact that the majority lasted longer than forty eight hours was an index of the severity of the established condition As my article is primarily psychiatric, the rather confusing statement about their change of obstetric practice in 1951 is not germane to the issue

Antenatal education and labour ward management, although interesting in themselves, were part of the clinical environment, and being similar for both groups ceased to operate as a significant factor in the production of dysfunction labour

I must dissociate myself from the ambiguous statement " we have also found that women who showed obvious overt anxiety during pregnancy would, after reassurance, have an average labour " May I quote from my own work ? " The results of this investigation, while not testing the hypothesis directly, do not offer any basis for believing that simple methods of psychotherapy, given in the antenatal period to outwardly tense or nervous women, would have had any effect on the action of the uterus during labour "

The letter ends with a quotation from Professor Nixon's paper to the thirteenth Congress of Obstetrics and Gynæcology in 1952 with which Dr Tylden contradicts my view that prediction was not possible I am afraid that my words have been misconstrued since my article clearly states " it is thought that *psychiatric* methods of prediction and prevention in the antenatal period would have no effect on the occurrence of uterine dysfunction My interpretation of the word " predict " seems to be much more exact than their more general terms, and of course I do not use the words " not possible "

Finally, I must refute the implication that we in Aberdeen are interested antenatally only in the purely mechanical elements of pregnancy and labour That this is not the case is surely manifest not only in the title of my work, but also in the nature of my specialty

May I turn now to Dr Reiss's letter (Feb 26) in which the criticism hinges on my statement that " fear, emotion, and anxiety play no part in the outcome of labour from the practical obstetrical point of view—i e , in determining the length of labour or whether forceps will b necessary "

His criticism is particularly based on the explanatory expansion which of course I could well have omitted It will now be clear that the phrase " whether forceps will be necessary " should read " whether operative interference will b necessary " Consequently there is no necessity for me t discuss the indications for forceps delivery

I can reassure him that the features he mentioned—planne pregnancy, length of marriage before conception, relati fertility, and previous abortions—were not ignored, but wer the same for both groups Relative fertility was specificall mentioned in my article as it was considered one of the mo important factors

I disagree with his assertion that " the puerperium, whe emotional tensions are notoriously heightened in man women, may be an unsuitable time for accurate psychologi assessment " Quite obviously the patients could not be se antenatally, nor always during labour On the contrary, feel that the puerperium with its heightened emotional tensio was excellent for my purpose in making material, particular of a sexual nature, much more freely available

I can make no comment on the purely obstetrical aspe of Dr Reiss's letter, which is not apposite to my study, b if he cares to re read my article he will find that I agree wi him about the importance of the mother's mental outlook

Kingseat Mental Hospital,
Newmachar, Aberdeenshire

W A CRAMOND

## HYPERGLYCÆMIA AFTER BURNING

SIR,—Dr Butterfield claims, in his article last we that dimercaprol (BAL) has a hypoglycæmic effect the hyperglycæmia which occurs in some burned patien The evidence upon which this claim is based is n convincing as the hyperglycæmia still persisted in h glucose dimercaprol tolerance tests Presumably he h distinguished the hyperglycæmia and glycosuria in h patients from the pseudodiabetic lactosuria and lact sæmia which may occur in patients whose burns a dusted with lactose containing medicament powder

Dr Butterfield also suggests that post burn hyp glycæmia is to be attributed " at first " to adren cortical hyper stimulation and that *early* involvement the islets of Langerhans does not take place Th former may be true but the latter should be treat with caution

In this department necropsies have been done on number of severely burned patients who had develop true hyperglycæmia and heavy glycosuria Histologic examination revealed that, in addition to evidence adrenocortical hyperactivity, many showed changes the pancreatic islet cells which cannot be attributed post mortem effects The following is a recent exampl

A girl, aged 5 years, suffered burns involving 50% of h body area and survived sixteen days Eleven days aft burning heavy glycosuria and hyperglycæmia were foun (blood sugar 380 mg per 100 ml.) The glycosuria (8-10 glucose) and hyperglycæmia were confirmed on sever occasions and the " sugar " was proved to be glucose Necrop was done twenty four hours after death Histological examin tion of the pancreas revealed that some of the cells in th islets of Langerhans had been destroyed or damaged and th regeneration was occurring The nuclear changes includ pyknosis hyperchromatism, giant nuclei, *mitoses*, and mult nucleation—none of which can be attributed to autolysis as well as bizarre nuclei karyolysis, and fragmentation

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[1] Blackburn E K King G M *J Fac Radiol Lond* 1954,

[1] Baar S Bull J P *Lancet* 1952 i, 978

Cytoplasmic changes include partial or total hyaline degeneration as well as swelling and disintegration There was also histological evidence of adrenocortical hyperactivity—namely almost complete loss of cortical lipoid and splenic eosinopenia[2]

These findings indicate that the diabetic state of burns is at least partly due to early pancreatic damage The presence of mitotic figures in the islet cells suggests that the damage may be reversible This would support Dr Butterfield's experience that the diabetic state after burning is often temporary

Pathology Department
Accident Hospital and M R C
Burns Research Unit Birmingham

S SEVITT

## PERFORATED PEPTIC ULCERS

SIR,—Mr Kirkman states (Feb 26) that 1 death which I included in the simple suture group (table II) should be included in the non-operative group because the case was treated conservatively But this patient was treated conservatively not from choice but because she was considered to be *too ill for operation* In other words when a particular method is being used all cases admitted in that series must be considered as of that series.

He also states that 5 of the 65 cases treated conservatively were unproved and should be discarded

While I cannot agree with this—for these were typical cases, and an absence of free gas shoulder pain and subsequent barium meal does not exclude a perforated ulcer—their exclusion only alters the percentages to 5% of deaths in the conservative group as against 4 4% in the simple suture group —an insignificant difference in a small series

Arising *from this* I would *agree with him that if only* one method is to be used in all cases, then simple suture is the safest I feel, however that each case of perforated ulcer should be considered on its merits and not forced into a standard mould *of treatment*

General Infirmary Leeds.

H D MOORE

SIR,—Mr Kirkman has interpreted my letter of Feb 5 in a way I had not intended I was not expressing an opinion as to the relative merits of operative and conservative treatment of perforations in general but merely questioning the validity of Mr Moore's statement vis-à-vis his own series. Mr Moore has already cleared up that point (Feb 12) and I would wholeheartedly agree with both Mr Moore and Mr Kirkman that operation is the treatment of choice

Department of Surgery
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Dundee.

JOHN GRIEVE

## CANCER CLUES

SIR,—Your annotation of Feb 19 prompts me to write to draw attention to our pathetic lack of knowledge about cancer ætiology and ecology The ignorance of the ecological circumstances is due less to the difficulty of approach to the problem than to an unjustifiable pessimism about the possibility of finding out new facts about cancer ætiology anywhere except in the laboratory

There is an urgent need for field teams possibly organised by W H O., to describe and calibrate the environments including in this context diet) in which different sorts of growth are found often or rarely Such teams would need to include (among others) personnel with special training in morbid anatomy statistics, sociology dietetic surveying and public-health administration The teams would work with the government health officials of the countries or areas to be studied, and local agencies would be used to help with the surveys Certain of the personnel need not be highly trained and the work would provide an excellent opportunity to medical students who wished to do some field research in an unfamiliar country When these workers returned to their own country they would have received a valuable stimulus to their curiosity and to their powers of systematic observation and of formulating and testing hypotheses. The results of standardised investigations of the habits and environment of different areas and, the varying incidence of different types of growth in them, would be correlated at a central headquarters establishment.

Another neglected approach to the problem of cancer causation is the use of the questionnaire for a controlled series of patients and normal people This method which uncovered the association between smoking and lung cancer, should be in the widest use at present for testing hypotheses on ætiology which clinical experience may suggest

It has surprised me to learn that detailed mapping of cancer incidence in this country has hardly begun and the pioneer work of Dr Percy Stocks for the British Empire Cancer Campaign should be an example to every regional hospital board or area health authority The need today is for as many people as possible to start *guessing and trying or to put it differently to start making hypotheses about environmental factors in ætiology and then to test these statistically* Regional boards could make a useful investment by each appointing *a statistician for research into cancer ætiology*, to work with medical officers of health and other doctors in the region

The causation of cancer is likely to remain a mystery unless more people learn to ask simple questions and to seek answers outside the laboratory

Mass X Ray Service for
South West London,
Grove Hospital S W 17

F A NASH

## SANATORIA

SIR —Dr Stradling's suggestion (Feb 19) that the trend in the treatment of *tuberculosis* is toward clinic management gave rise to four most interesting letters last week

While agreeing with many of the points in these four letters and also the restrained wisdom of Mr Temple (Jan 8) I think that Dr Stradling is right Granted that remoteness is only one factor leading to the closure of the Trudeau Sanatorium, it is nevertheless, a fact that the Royal National Sanatorium at Ventnor a fully equipped chest hospital in every way has for some months had empty beds, which can be accounted for only by the inaccessibility of the Isle of Wight Nowadays many patients are not willing to take their treatment a long way from home

Formerly local health authorities made provision for sanatorium treatment and patients could either take it despite distance or leave it From data which I published in 1947 referring to the previous thirty years in a county borough, it appeared that 52% (367 out of 706) sputum positive stage I or stage II cases in that town never had sanatorium treatment Among the various possible *reasons* for this, one was that the available sanatorium was 90 miles away It is the local chest physician who has to persuade the patient to go to a perhaps distant sanatorium and to answer the anxious pertinent questions as to the *necessity* for this.

I cannot agree that a sanatorium doctor looking *after* a patient for a year or so necessarily gets to know him better than the diligent clinic physician who should become the guide counsellor and friend to the patient and his family for many years

I agree with Dr Stradling that antibiotics have now *become a* more important item in treatment than strict bed rest (How many sanatoria still impose ' absolute rest ?) Few of us have yet adopted ambulant drug treatment as extensively as Dr Pritchard (Feb 5) but it seems entirely reasonable that carefully chosen cases be treated in this way

Nowadays at least *50%* of patients with pulmonary tuberculosis whose *disease* needs active treatment require essentially a period of antibiotic drugs and withdrawal from their ordinary mode of life with later consideration of major surgery If their home conditions are good *many of these* people welcome the continuation of their

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2. Sevitt S *J Path Bact* (In the press)

medical care at home after an initial period in hospital to teach them about their disease—especially if their illness is likely to last over a year and culminate in surgery Even in the best sanatoria it is not easy to keep morale high for twelve months or more Many cases can be supervised in this way under " clinic management " provided that the clinic is fully equipped and well staffed There is nothing new or revolutionary about having tuberculosis wards in local general hospitals The London County Council and other local authorities were doing it for years before the National Health Service came along

The bare economics of the hospital service will not enable us to dispense with our biggest and best-equipped chest hospitals Some of these have, for historical reasons, developed in rustic parts of the countryside, but they are first rate medical and surgical centres and for a long time yet there will be tuberculosis patients in need of them There are other institutions, though, which are merely country convalescent homes capable of caring for coughing consumptives As the need for tuberculosis beds diminishes some of these must be the ones to close

Certainly the chest physician in the clinic, busy with diagnostic problems and other diseases to treat, as well as having many opportunities for following the fascinating epidemiology of tuberculosis and its prevention, has plenty to do besides managing the inpatient and home treatment of the disease But it seems certain that better staffed chest clinics and still closer integration with local hospitals is the way in which the chest service in this country will develop

Bournemouth Chest Clinic. W H TATTERSALL

## HYDROCORTISONE OINTMENT IN DERMATOSES

SIR,—Hydrocortisone ointment has been reported from the U S A to be beneficial in pruritus ani [1] and in various dermatoses [2] Small series of successfully treated cases have also been reported from Europe [3] [4] Only two such accounts have so far been published in Britain [5] [6]

In the past four months I have used this ointment in selected skin diseases at the dermatological clinics in Ayrshire 42 cases of selected dermatoses in adults have been treated and followed for four months The ointments used were 2 5% and 1% hydrocortisone acetate in a water-miscible, non-greasy, propylene and polyethylene-glycol base, supplied by Roussel Laboratories Ltd No control ointments were used, since 40 of the 42 cases had previously been treated unsuccessfully with various other ointments The results are shown in the accompanying table

*Pruritus*

In the 22 cases of pruritus local causes of itching were excluded before treatment was started Only 1 patient had not previously been treated , and the disorder had been present in these cases for from five months to fifteen years Each patient was instructed at the start of treatment to apply the ointment with gentle massage to the affected areas, twice daily On starting, one 5 g tube was given, to last one week , and this was continued for three weeks Subsequently one 5-g tube of ointment was given every two weeks or as required The response was excellent in 16 cases In these 16 the 2 5% ointment was used for six weeks and then stopped completely or replaced by 1% ointment, which was applied only every two or three days 4 patients have been off treatment for eight weeks without recurrence of itching A very good result was noted in another 4 cases In this group itching ceased, but the 2 5% ointment still has to be used for continued relief In both of these groups the response was rapid, and itching ceased within seven days of starting ointment In 1 patient with pruritus vulvæ initial impr ment was very good but itching returned within four wee And although it is less intense it has persisted In the 1 pat who became worse pruritus ani had been present for ten y and the perianal skin was sodden and macerated After days of treatment the skin became infected and deep-se pustules formed

RESULTS IN 42 CASES

| Disorder | No of cases | Results | | | |
|---|---|---|---|---|---|
| | | Excellent | Very good | Improved | W |
| *Pruritus* | | | | | |
| Anal | 15 | 10 | 4 | | |
| Scrotal | 3 | 3 | | | |
| Vulval | 4 | 3 | | 1 | |
| Lichen simplex | 10 | 6 | 2 | 1 | |
| Atopic dermatitis | 6 | | 2 | 3 | |
| Nummular eczema | 4 | 2 | 1 | 1 | |

*Lichen Simplex*

10 cases of lichen simplex chronicus were treated disorder had been present for from six months to four ye The result was excellent in 6 cases and very good in 2 Ano patient, although benefiting from the ointment, was entirely freed of itching and required daily treatment 2 5% ointment The last patient in this group became wo and within ten days the area on the back of the neck impetiginised In 3 of the 6 patients showing excellent res treatment has been suspended for eight weeks with no re rence of itching, while the other 3 cases require intermit treatment with a 1% ointment

*Atopic Dermatitis*

6 cases of atopic dermatitis were treated All were of duration and wide extent The skin cleared completel no case , but in 2 the results were very good, with abaten of lichenification, excoriation, and itching , daily applicatio 2 5% ointment in 1 case, and of 1% ointment in the ot was necessary to prevent recurrence In 3 cases the cond of the affected skin improved, but the skin remained slig lichenified In the 6th case folliculitis developed on the w and antecubital fossæ after eight days' treatment

*Nummular Eczema*

4 cases of widespread nummular eczema of at least months' duration were treated. The results were excellen 2 cases, with rapid disappearance of the lesions and no re rence six and eight weeks after stopping the ointm Another patient showed complete clearing, but relapsed weeks after withdrawal of the ointment, and now requ regular application of the ointment The last case, altho much improved, did not clear completely , daily applica of ointment was necessary, and treatment has now b abandoned in this case

In this small series of 42 cases of selected dermato the results were excellent or very good in 33 , and of the 33 patients had been previously treated with li success

For rapid initial improvement, a 2 5% concentrat of hydrocortisone acetate is the more effective, althoug 1% concentration often suffices to maintain subject and objective improvement The ointment is easy apply It does not sting or burn and does not st clothing or bed linen The index of skin sensitisation hydrocortisone acetate is low, and no instance of sensit tion was found in this series If sensitisation does app the base rather than the hydrocortisone should suspected

Smith [7] showed that there was lack of experimen evidence that hydrocortisone acetate applied topica was absorbed in significant amounts Sulzberger Baer [8] state that in many hundreds of cases there been no systemic upset from local application of hyd cortisone even after prolonged use over wide areas would appear, therefore, that hydrocortisone ointm relatively safe No side-effects were observed in any these 42 patients

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[1] Alexander, R M Manhelm, S D *J invest Derm* 1953, 21, 223
[2] Sulzberger M B Witten V H Smith C C *J Amer med Ass* 1953 151 468
[3] Sidi E Bourgeois Gavardin J , Plas, G *Pr méd* 1953, 61 992
[4] Hellesen, B Kristjansen A., Reymann F *Arch Derm Syph , Chicago* 1954 70 360
[5] Malkinson, F D Wells G C *Brit J Derm* 1954, 66, 300
[6] Church R, *Brit med J* Feb 26 1955 p 517
[7] Smith, C C *Arch Derm Syph , Chicago,* 1953 68, 50
[8] Sulzberger M. B , Baer R. L *In* Year Book of Dermatol and Syphilology, 1953–1954 Chicago, 1954

No distant effect of the hydrocortisone acetate was erved in this series, although Sidi et al [3] found that as removed from those treated with ointment ponded to the hydrocortisone

The disadvantages of treatment with hydrocortisone etate ointment are: (1) lessening of the resistance of e tissues to infection; and (2) the tendency of the ions, in many cases to relapse after treatment has been continued Prolonged use of the ointment may avert ese relapses, and a combination of the hydrocortisone th an antibiotic may control infection

The relatively poor results in atopic dermatitis and ummular eczema compared with the results obtained Sulzberger et al.[3] in these diseases, may be accounted by the smallness of the supply of hydrocortisone at y disposal.

Heathfield Hospital,
Ayr County Area.

THOMAS COCHRANE
Consultant dermatologist

## MOLLUSCUM PSEUDOCARCINOMATOSUM

SIR,—The interesting article by Dr Martin Beare Jan. 22) and the letter by Dr Church (Feb 26) prompt e to report the only case which I have seen in which e lesion recurred after treatment but subsequently sappeared spontaneously

A man, aged 33 was seen on March 6 1953 with a typical olluscum on the right cheek. It had first appeared two three weeks earlier at a point where he had cut himself having It had grown rapidly and had attained a diameter 1·4 cm. and it projected 4 mm. from the surface of the rrounding skin. After a formal biopsy including both edges the lesion, it was treated by simple curettage followed by ht cauterisation, sufficient only to produce hæmostasis. Histological examination confirmed the diagnosis of molluscum eudocarcinomatosum, but on March 27 1953 the lesion ad recurred and measured 1 2 × 1 3 cm No further treat ment was given and on May 8 1953 the area was flat and ry When the patient was last seen on July 3 1953 there as merely the depressed, rather irregular scar such as one ually seen.

One is tempted to wonder whether spontaneous recovery might have occurred if no further treatment had been given in the cases reported by Dr Beare and Dr Church These recurrences may perhaps be explained on the basis of infection With most of these lesions as with warts simple removal is usually enough to stimulate the natural defence mechanism of the skin The cases which have recurred were all treated relatively soon after they appeared possibly before sufficient immunity had developed

Finally I should like to support Dr Beare's plea that these lesions should be distinguished from squamous epithelioma and that the patients should be spared from unnecessary heavy irradiation

Exeter

J R SIMPSON

## TREATMENT OF STEATORRHŒA

SIR,—Since patients with fatty stools often have abdominal discomfort simple alterations in régime directed to reducing the fat in their stools are worth trial.

I have under my care a man, now aged 20 who following a road accident had the greater part of his small intestine removed at operation only the duodenum and some 18 inches of jejunum remains. There was difficulty in maintaining his nutrition, and his stools contained a gross excess of fat It was pointed out to me by Dr J N Hunt that hydrolysis of butter fat yields a higher proportion of short-chain fatty acids than other culinary fats The short-chain fatty acids are more water-soluble than the long-chain fatty acids and it may be presumed that they are more readily absorbed from the small intestine The patient was therefore given a diet containing generous quantities of butter but all other forms of fat were avoided. The patient has now been under observation for two years; his general nutrition remains excellent, and he has shown neither decalcification of the bones nor anæmia. He has had no other treatment It is hoped later to publish a detailed surgical and metabolic study of this patient

The apparent success of this diet led me to try it in two cases of idiopathic steatorrhœa, with the most satisfactory results in a patient with fatty stools due to pancreatic obstruction from a carcinoma there was a little temporary benefit

These observations are few and incomplete, but the diet is a simple one, and others may care to try it in patients with this distressing condition

London W 1

W N MANN

## BEHÇET'S SYNDROME

SIR,—Mr Phillips and Mr Scott (Feb 19) do not mention ethisterone or progesterone amongst the many remedies they have tried for the relief of Behçet's syndrome I have had good results in a case with premenstrually exacerbated oral ulceration, associated with rheumatoid arthritis by giving 20 mg ethisterone three times a day, during the fortnight preceding menstruation The vulva and eyes were unaffected in this case but I do not doubt that it represented this syndrome in an incomplete form I suggest that this drug, which is readily available and cheaper than cortisone and corticotrophin be tried in cases exhibiting premenstrual exacerbation since all other drugs appear to have been without effect

Dulwich Hospital,
London S E.22.

BERNARD FREEDMAN

SIR,—I was interested in the article by Mr Phillips and Mr Scott There is no doubt that the syndrome is commonly present in partial form—mouth ulcers only In the complete syndrome a history of previous mouth ulcers is not uncommon Only the new development in the eye or on the genitals brings the patient to the doctor

Some of these patients get acute dyspepsia at the time of the mouth ulcers, but out of proportion to the dysphagia due to a sore mouth. It would be interesting to know whether acute gastric ulceration has in fact been seen Some time ago I saw a man who had bouts of acute dyspepsia lasting two to three weeks accompanied by mouth ulcers—often quite trivial This may not be uncommon I believe one paper on mouth ulcers gave as a title yet one more name for this condition — dyspeptic ulcers.

The genital lesions can be severe and can as Mr Phillips and Mr Scott mention occur high in the vagina One patient I saw had been off work for a year and had been unable to walk for months

Chester

G P B WHITWELL.

## HYDROCORTISONE IN LESIONS OF SOFT TISSUE

SIR —Several points in last week's paper by Dr Crisp and Dr Kendall invite comment

The authors claim in their summary to have treated '200 cases of soft tissue lesions by local injection of hydrocortisone In actual fact these cases were treated by injection of 2–5 ml. of a lytic cocktail consisting of hydrocortisone 2% procaine hydrochloride and hyaluronidase Many of the conditions listed have been treated by others with considerable success by injections of either hyaluronidase procaine hydrochloride or a combination of both It would therefore seem very unwise to ascribe the dramatic results of their injection treatment to the effects of hydrocortisone alone

There do not appear to have been any controls *in their* series of cases and in only 4 instances are details of treatment and the clinical response given The true value of hydrocortisone could have been easily *determined* if these 4 patients had been treated by injection locally of other solutions such as procaine hydrochloride and then at a later date given an injection of hydrocortisone

Certain conditions are listed which could not be reasonably expected to respond to *injection* therapy and good results are claimed. *Trigger finger for instance* is generally accepted to be a condition in which the disordered finger movements are due to a very definite mechanical defect *for* which the only satisfactory treatment is surgical exploration and release of the obstructing factor It is conceivable that simple tenosynovitis, especially of the acute variety, might be improved by a local injection of hydrocortisone with or without the addition of hyaluronidase and procaine, but this I submit, is not the condition known as trigger finger

The authors claim that of 6 patients with Dupuytren s contracture treated in the early stages 4 could fully extend the affected finger after the injection of hydrocortisone No details are given but it would be very interesting to know which part of the contracted palmar fascia was injected and also what were the symptoms for which the patients sought relief in the first place The natural history of Dupuytren's contracture is such that it would be unwise to make any conclusions after a follow up interval of only two months Some cases lie dormant for many months or years before showing progression others can be kept in check for many months or years by intermittent splintage at night, some progress so rapidly as to mimic a malignant disease process It would be interesting to know to which category those cases belonged that were treated by injection of hydrocortisone

The enthusiasm of Dr Crisp and Dr Kendall commands respect, but the evidence given in its present form does not, in my opinion, justify the widespread use of an expensive drug about whose effects we know surprisingly little

Plastic Surgery Centre
St Lawrence Hospital
Chepstow Mon

MICHAEL N TEMPEST

## ANTITUBERCULOUS ACTION OF 1,3,4-OXDIAZOLONES

SIR,—As Barry and Conalty[1] have pointed out, isoniazid, and derivatives of isoniazid such as *o* hydroxybenzol isonicotinyl hydrazone ('Salizid'), readily permit the growth of resistant variants of H37Rv when the organism is grown in vitro in the presence of concentrations just insufficient to restrict growth Knox et al,[2] Barnett et al,[3] and Barry et al[4] have all shown how readily strains of *Mycobacterium tuberculosis* resistant to isoniazid can be produced in vitro

In the course of work on the new 2 pyridyl-1,3,4-oxdiazolone (5) reported by Wilder Smith,[5] we investigated the production of variants of H37Rv resistant in vitro to isoniazid and to the oxdiazolones We found that H37Rv grown in the presence of 2 pyridyl-1,3 4 oxdiazolone (5), or its *p* aminosalicylate, does not develop any signs of resistance even after six months' subculturing at fortnightly intervals In parallel control experiments with isoniazid, resistance was produced comparatively rapidly

Liquid Dubos media were used without the addition of 'Tween' or oleic acid for all cultures except the first one The tuberculostatics were added to give concentrations of 0 001, 0 01, 0 1, 1 0, 10 0, 50 0, and 100 µg per ml The first subculture was inoculated with one drop from a Pasteur pipette taken from a fourteen day Dubos Tween culture (H37Rv) All subcultures were made after twelve days' incubation, and inoculated into fresh media containing the tuberculostatic in question The material for subculture was taken from the last tube in which unrestricted growth occurred All tests were carried out in duplicate the first series of tests covered 9 subcultures and the second 6 subcultures

Both series showed clearly that resistance is rapidly produced to isoniazid The sensitivity of the original culture to isoniazid was 0 001 µg per ml After the seventh subculture the sensitivity was 0 1 µg per ml and after the ninth subculture 50 0 µg per ml The sensitivity of H37Rv against 2 pyridyl (4) 1,3 4 oxdiazolone (5) and against its *p* aminosalicylate however, remained practically constant at 0 1–1 0 µg per ml up to the sixth and ninth subcultures These results have been confirmed by others interested in the pyridyl oxdiazolones

Not only was it impossible to produce resistance to the pyridyl oxdiazolones by subculturing in vitro but it was also found that these substances showed activity against all the resistant strains of *M tuberculosis* which we investigated.

Clinical trials of the new compounds were carried out over six months on 70 patients, a large number of whom were no longer responding to *p* aminosalicylic acid, streptomycin, isoniazid, and in some cases terramycin A definite response was observed in a number of cases, which tends to confirm the in vitro observations

Cantonal General Hospital,
Lucerne, Switzerland

H BRODHAGE

## THE PATHOLOGY OF REHABILITATION

SIR,—Dr Fowler is to be congratulated on highlighting, in his article last week, problems with which many of us have been grappling for some time His findings bear out the impressions which have been formed in the course of daily work

This article is a strong argument for extension of the occupational health services The presence inside an industry, as part of that industry, of a doctor who has the trust of management and men is the best way of ensuring that employees are fitted in to tasks appropriate to their abilities and that the progression of recovery through work is carefully followed

There are two other small points I should like to make

Dr Fowler says that the dangers of the employment of epileptics have been exaggerated If he means the physical dangers no one *will argue but it is a fact that recent court* decisions have made many employers wary of accepting an increased responsibility, which has been clearly laid at their door in the event of some unforeseen accident

The second point concerns "the neurotic element in physical disease" This is hard to define and any classification is bound to be arbitrary, but it is the deciding factor in nearly every case and one cannot help feeling that the medical profession is not blameless The "light work" or 'no night shift" certificate which gives no indication of how long the restriction is to be imposed has proved as disabling as any physical syndrome It disheartens patient and employer alike and should be most sparingly used

Many industries re employ their own handicapped very successfully without elabortae facilities, and a good occupational health service should make this a prime duty

K P DUNCAN
Chief Medical Officer
South Western Gas Board

Bath

# Parliament

## QUESTION TIME

### Recruitment of Nurses

Mr V J COLLINS asked the Minister of Health in how many regions the recruitment of nurses had been suspended or reduced because of the instruction to hospital management committees that recruitment of nursing staff up to approved establishment could only be made on condition that the salaries of staff so recruited could be met from the approved estimates —Mr IAIN MACLEOD replied Full information is not available, but it is obvious that improvements and developments including increases in staff, can only be made if the cost can be met within the allocations One of the main items in the new moneys for which the different authorities have asked is, of course, their expectation of increasing the numbers of staff available to them

Mr R W SORENSEN asked whether the Ministry could try to transfer some nurses from the overstaffed hospitals to some understaffed hospitals —Miss PATRICIA HORNSBY-SMITH A certain amount has been done by the standstill of establishments with just that result There is an improvement, but not in the mental hospitals That method has helped the other hospitals It is fair to say that the staffing figures for the general and teaching hospitals are not wholly comparable with the others

### Trainee Nurses

Dr BARNETT STROSS asked the Minister whether he was aware that at some hospitals trainee-nurses were engaged for long periods on night duty, and what were the exact recom

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1 Barry V C Conalty M L *Lancet* 1954 ii 494
2 Knox R King M B Woodroffe R C *Ibid* 1952 ii, 854
3 Barnett M Bushby S R M Mitchison D A *Ibid* 1953 i 314
4 Barry V C Conalty M L Gaffney F *Ibid* p 978
5 Wilder Smith A E *Science* 1954 119 514

ndations laid down by his regulations on this point — HORNSBY-SMITH replied: The Nurses Salaries Committee commended that student nurses should not be employed tinuously on night duty for longer than three months Minister is aware that it may not always be possible to erve this recommendation There are no other require ts on the subject

Replying to a further question Miss HORNSBY SMITH said the Minister had made no regulation on the time allocated student nurses to attend lectures. He thought it best to e the arrangements to the discretion of hospital management committees and boards of governors but whenever ble student nurses should not in his view be expected attend lectures in their free time

### Mercury in Teething-powders

Replying to a question Miss HORNSBY SMITH said the ister had considered the recent case to which his attention drawn, of a baby's death from mercury poisoning While Minister was advised that mercurial preparations had a er place in medical treatment his medical officers had dy suggested to medical officers of health that powders taining mercury should be issued from child welfare clinics on medical advice and with precise instructions He ld consider further whether to suggest that these preparations should cease to be available at clinics at all

Mr B T SWINGLER In addition to the action proposed the Minister not agree that some general public warning ht be sent out by the Minister's medical advisers in view the public concern created by recent inquests?—Miss NSBY-SMITH I think that the general publicity particu in professional journals and advice given by the Minister's ical officers of health has made this clear I should like ke it plain that if they were not given by clinics that ll not interfere with the right of a doctor to prescribe paration in which mercury was included

### Tuberculosis Treatment in Swiss Sanatoria

Replying to a question Mr MACLEOD said that 140 patients England and Wales were now being treated for tuberculosis in Swiss sanatoria under the National Health Service

### Registration of Opticians

Replying to a question Miss HORNSBY SMITH said that the ister could hold out no hope of introducing legislation for registration of ophthalmic and dispensing opticians ent.

### Food poisoning

Mr SOMERVILLE HASTINGS asked the Minister of Health many food poisoning incidents due to processed and up meats were recorded in 1950 1951 1952 and 1953 what percentage of the total incidents resulted from such in each of the four years.—Mr MACLEOD replied: following table gives the number and percentage of ed outbreaks of food poisoning—i e instances of two more related cases, but excluding sporadic cases where essed and made up meats have been identified as the of infection

| Year | Number of outbreaks attributed to processed and made-up meats | of total outbreaks (all foods) where the vehicle of infection has been identified |
|---|---|---|
| 1950 | 20* | 46 |
| 1951 | 114 | 18 |
| 1952 | 144 | 33 |
| 1953 | 104 | 53 |

### Pharmaceutical Imports

Replying to a question Mr PETER THORNEYCROFT President of the Board of Trade said he was aware of the heavy se in the value of imports of medicinal and pharmaceutical products during 1954 as compared with 1953 The to which this increase was due to increased imports from United States of America was nearly 60%. He imagined the imports had increased because some of the new had been developed and produced in the United States, he thought it was right that people in the United Kingdom ld have access to them He was anxious to conserve dollar resources but he thought that the Government ld hesitate before restricting the import of up-to-date for healing sickness

## Obituary

### EDWARD VIPONT BROWN

M.D Lond

Dr Vipont Brown, who died on Feb 26 at the age of 92 had practised in Manchester for nearly sixty years

He was born in 1863 of Quaker stock at North Shields, where his father was a doctor At Bootham School York, he broke the record for the mile and began an interest in football and cycling which included a journey from York to Edinburgh on a penny farthing He trained at St. Bartholomew's Hospital at a time when gynæcologists called in a surgeon to operate on their cases, and where he was taught to laugh to scorn the teaching of Lister who had recently come to King's College Hospital to convince the London surgeons of the value of his methods He was even upbraided when he cut his hospital lectures to listen to those given by Lister He qualified in 1886

In 1891 he went to Manchester "just for a fortnight to help a friend" and he stayed in practice there for over half a century taking his M.D in 1901 In his early days he would return from his rounds by horse tram, and he was probably the last doctor in Manchester to wear the traditional top hat and frock coat. Long before he retired he was one of the most respected and best liked general practitioners in the city He was a family doctor in the widest sense of the word and made every effort to keep up to date in his methods and treatment attending regularly postgraduate lectures and demonstrations until he was well over 70 He did much pioneer work in the medical services of the city especially in connection with district nursing

Deeply religious he was a leader of the Quaker community writing articles on Quaker Aspects of Truth, temperance and for the Fabian Society in 1910, a pamphlet on *The Medical Profession its present work and its future* He was a lifelong and fearless campaigner for peace He retired from practice on his 83rd birthday and left Manchester with his wife to live with their daughter at Yealand Conyers. There last month they celebrated their diamond wedding The practice continues in the hands of his son

### Dr O T AVERY

R M H a former resident physician to Avery's respiratory service in the Hospital of the Rockefeller Institute writes:

> My introduction to the work of the service was a week in conclave with Fes when he expounded to me his whole concept of pneumococcal pneumonia and the immunity of the subject starting from the point when he and Do (Dochez) decided to take the pants off the pneumococcus going systematically through the experimental work of Heidelberger Goebbel Dubos Francis Horsfall and McLeod His explanation had the fantasy of J M. Barrie—whom he was not unlike but he had no moustache—and his tenderness and sense of feeling were manifest by the fact that he would never visit any patient Yet every detail of the patients under our care was known to him and during the time I was there not one with pneumococcal pneumonia was lost We were then using antipneumococcal serum and the sulphonamide era was just dawning
>
> 'Lunch with Fes in the institute was an exciting and exhilarating experience It often lasted until well after three during which time he would unravel his theories on immunochemistry Experimentally he demanded the highest standards and everything had to be done by oneself a principle he shared with Landsteiner though as men they were poles apart Hurricane Edna kept me from seeing him last September but his delightfully whimsical temperament his puckishness, his sincerity and his profound philosophy will remain as bright a light as the torch held by Liberty at the entrance to New York harbour

## Births, Marriages, and Deaths

### MARRIAGES

CASSON—SEMMEL.—On March 5 in London, Dr Frederick Ronald Christopher Casson to Mr Ilse Semmel

MURPHY—THOMPSON.—On Feb 19, Grahame Edward Murphy M.B., M.SC., F.R.C.S., to Isabelle M Thompson M.B., L.D.S.

# Notes and News

## NEW END THYROID CLINIC AND DEPARTMENT OF ENDOCRINOLOGY

On March 2 the Duke of Edinburgh formally opened this department at New End Hospital The chair was taken by Mr John Fremantle, chairman of the North West Metropolitan Regional Hospital Board, which first began the extension of the department by setting up a radio isotope laboratory two years ago Among those present were Mr Iain Macleod, the Minister of Health, and Sir Thomas Dunhill, founder of the London County Council Thyroid Clinic from which the new department has developed The Duke of Edinburgh was conducted through the new premises, housed in the shell of the old maternity unit, by Mr J E Piercy, the surgeon superintendent of the hospital, and Dr Raymond Greene, senior physician to the hospital and the originator of the extension plan The new department has 26 beds, a new biochemical laboratory, an extended and improved radio isotope laboratory, an outpatient department, and a new operating theatre, all in convenient juxtaposition. The transmutation of the thyroid clinic into a complete endocrinological research unit has been made possible by a gift from King Edward's Hospital Fund Messrs Organon are giving an annual subsidy to the research work of the department

## CONVERSION OF PRINCESS LOUISE HOSPITAL

Mr Iain Macleod, the Minister of Health, announced in the House of Commons on March 7 that no final decision had yet been taken regarding the proposed conversion of Princess Louise (Kensington) Hospital to adult use[1] The proposal, made originally by the coördinating subcommittee of St Mary's Hospital board of governors, was endorsed by the board on Feb 24 Two days earlier the Kensington and Hammersmith division of the British Medical Association had unanimously adopted the following resolution

> "Being satisfied as to the continuing needs of sick children in the area the medical practitioners of the Kensington and Hammersmith district ask the Minister of Health to give serious consideration to the necessity for the Princess Louise Hospital to continue as a children's hospital serving the needs of the area We would further like to impress on the Minister that these needs should take priority over the teaching requirements of St Mary's Hospital"

This resolution was endorsed by the medical staff of Princess Louise Hospital, who drew attention to similar resolutions passed by the council of the Royal Borough of Kensington and by Hammersmith borough council Earlier, the association of friends of the hospital had written to the Minister pointing out that the hospital, which had served the borough of Kensington for 115 years, was the only children's hospital in a very densely populated area[2]

## GUY'S HOSPITAL DENTAL SCHOOL

The annual clinical meeting of the school, on March 5, once more showed the growing use of visual aids to teaching and of colour cinematography in recording the progress of orthodontic patients Mr E Gwynne Evans's record film, assembled from shots taken during the past five years, made clear the importance of the relation between orofacial muscular behaviour and malocclusion Electromyography is now being used to study both normal and abnormal muscular patterns

Dr D J Anderson demonstrated his method for determining the pressure developed between the teeth during chewing, he uses a small resistance strain gauge held in the tooth by a specially designed inlay Preliminary calculations suggest that a normal tooth is subjected to a thrust of some 15 kg during mastication, the thrust on an artificial tooth is only about 4 kg It is not thought that denture wearers chew their food less thoroughly, but that they have to make more jaw movements to achieve the same result Mr A C Kerr has devised an apparatus for collecting and measuring samples of saliva by inserting a fine 'Polythene' cannula in the duct of the parotid gland

Prof A B Macgregor, in his lecture on Antiseptics and Antibiotics, affirmed that only three antiseptics are of use in the mouth—tincture of iodine, proflavine, and cetrimide He considered that the sulphonamides, despite their disadvantages, should be used more in dental practice they are cheap, can be administered orally, and are effective against most pyogenic organisms Because of its low toxicity and because it can be injected locally, penicillin is still the mo valuable of the antibiotics, despite the increase in drug sensitive patients and in resistant strains of bacteria Befor a dental operation, for instance, a single troche of penicilli will, in 15–20 minutes, reduce the bacterial content of th mouth to about a fifth of its previous level The new antibiotics, with the possible exception of oxytetracycli are, in his view, too toxic for routine use

## HOSPITAL COSTS IN SCOTLAND

In Scotland during the year ended March 31, 1954,[1] t average cost of maintaining a patient in hospital, excludi specialists' salaries and overhead charges for empty be was £8 4s 3d per week, distributed as follows

| | £ | s |
|---|---|---|
| Patients food laundry, and clothing | 1 | 5 |
| Drugs, dressings and surgical appliances | | 10 |
| Staff salaries and wages food, laundry, &c | 4 | 3 |
| Domestic repairs, heat, light, power &c | 1 | 8 |
| Maintenance of buildings and other overheads | | 11 |
| Board of management administration | | 7 |

The average weekly costs of maintaining and treating patient in the different types of hospitals for the two ye 1952–53 and 1953–54 were

| | 1952–53 | | | 1953– | |
|---|---|---|---|---|---|
| | £ | s | d | £ | s |
| *General hospitals* | | | | | |
| 1–50 beds | 9 | 10 | 2 | 9 | 12 |
| 51–300 beds | 10 | 6 | 3 | 10 | 11 |
| Over 300 beds | 11 | 10 | 3 | 11 | 5 |
| Teaching | 11 | 3 | 1 | 12 | [illegible] |
| Maternity | 15 | 7 | 3 | 15 | 8 |
| Convalescent | 5 | 2 | 10 | 6 | 9 |
| Sanatoria | 8 | 11 | 7 | 8 | [illegible] |
| Infectious diseases | 9 | 18 | 1 | 10 | 13 |
| Mental | 4 | 14 | 2 | 4 | [illegible] |
| Mental deficiency | 4 | 7 | 7 | 4 | [illegible] |

The average cost of treating an outpatient was 4s 1 per attendance Attendances totalled 5,368,182

## HOSPITAL PHARMACEUTICAL SERVICES

In November, 1951, a subcommittee of the stand Pharmaceutical Advisory Committee, under the chairmans of Sir Hugh Linstead, set out "to review the arrangem for the provision of pharmaceutical services in hospitals to advise on the most efficient and economical organisa of those services" Their findings were summarised in report of the Central Health Services Council for 1953,[2] are now published in full[3] The Ministry of Health, draw the attention of hospital authorities to those of subcommittee's recommendations which it has accep suggests[4]

(1) That extraneous duties—such as the care and issue medical and surgical equipment or the operation o central syringe service—should be undertaken pharmaceutical departments only when there are str reasons for not making other arrangements

(2) That each pharmaceutical department should be un the charge of a qualified pharmacist, if a full t pharmacist is not employed, then one from the hosp group should be made responsible for supervising pharmaceutical service

(3) That regional boards and hospital management co mittees should investigate the possible advantages organising their pharmaceutical services on a gro basis, or even on one involving several groups.

(4) That each regional board should consider setting up pharmaceutical committee to advise them on matt of regional interest and to suggest ways of making pharmaceutical services more efficient and economical

(5) That, in view of the present shortage of pharmacis committees and boards should ensure that pharmac are employed only in positions which justify th training and skill, and which involve no duties that co be left to others less well qualified

(6) That manufacture of pharmaceutical preparations whether by individual hospitals or by hospital grou —should be undertaken only if justified on econom grounds

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[1] See *Lancet*, Jan 29 1955 p 241
[2] *Kensington News*, Feb 25 1955

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[1] Department of Health for Scotland Analysis of Running Co of Hospitals, year ended March 31, 1954 H M Statione Office 1955 Pp 63 9s 6d
[2] See *Lancet* 1954, ii 131
[3] Ministry of Health Central Health Services Council Repo of the Subcommittee on the Hospital Pharmaceutical Serv H M. Stationery Office 1955 Pp 40 2s
[4] H M (55)22

That groups where expenditure on infusion fluids exceeds £1600 annually should arrange to produce these them selves, since there is reason to suppose that this would be cheaper

Ministry also advises on the provision of research and ng facilities on the siting and planning of pharmaceutical tments, and on matters relating to liaison between the aceutical department and the nursing staff Some of ubcommittee's recommendations are still under con tion.

## A FAMOUS HOUSE

oxeric history of a firm as sympathetic to doctors as Allen & Hanburys is a pleasant thing to read In gh a *City Archway*[1] Desmond Chapman Huston and C Cripps bring these fabulous names to life in a le which begins in 1715 in Old Plough Court—where ms Bevan a Quaker had an apothecary's shop—and (but does not end) with a world wide industrial ation built by the able and humane characters who shaped its destiny

## CERTIFICATION OF BLINDNESS

Minister of Health after consultation with the Faculty phthalmologists has recommended to local authorities in and that all applicants for admission to the Register of Blind or the Register of the Partially Sighted should be fied only by ophthalmologists of consultant status.[2]

therto certification has been by doctors engaged whole time in halmology or in charge of the ophthalmic department of a al hospital of not less than 100 beds or (where the services of a practitioner could not reasonably be obtained) by a doctor ng a diploma in ophthalmology

he form of notification (form B D 8) has been amended to the certifying ophthalmologist to recommend in the of persons under 16 years the appropriate type of school the patient. The new form will enable the Ministry more ly to analyse statistically the causes of blindness.

## LITIGATION IN SCOTLAND

1954 claims against members of the Medical and Dental ance Union of Scotland again increased in number The s annual report[3] discussing this growth in litigation n attention particularly to median nerve palsy after y injection of anæsthetic solutions by inexperienced and pervised house-officers. When in such circumstances a l action ensues it is difficult says the report to establish atisfactory defence for usually no mistake would have n had the proper precautions been observed.

During the year membership rose by 100 to a total of Claims paid amounted to £3503 including one sum £2750

## SINDROME POLICARENCIAL INFANTIL

1951 F.A.O and W.H.O commissioned Dr J F Brock Dr M Autret to tour the African continent and report the nutritional disorder known as kwashiorkor Their rt[4] established that the disease was widespread in Africa d that local names in use in many countries referred to a itional disorder of childhood differing only slightly from ashiorkor as originally described in the Gold Coast. In the same U.N agencies again sent out Autret this time Dr M. Behar to Central America and their report[5] ws that in most countries in this region a similar disorder ommon in the early years of childhood At least fifteen es have been used to denote the syndrome in Latin erica, but now *sindrome policarencial infantil* appears to enerally established and it is unreasonable to expect nish-speaking physicians to learn the word kwashiorkor excellent clinical photographs and the descriptions of circumstances in which the syndrome arises in the deprived ill leave no doubt that the disorder is essentially the same Central America as in Africa This monograph which is lished in Spanish French and English editions should be of great value to all concerned with child health services in Central America. The bibliography which contains many references to Spanish papers little known in this country may be useful to pædiatricians and public health workers.

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[1] London John Murray 1954 Pp 326 25s.

[2] istry of Health. Circular 4/55

[3] dical and Dental Defence Union of Scotland Ltd., 105 t. Vincent Street Glasgow C.2 Fifty-Second Annual Report 1954

[4] Kwashiorkor in Africa. F.A.O Nutritional Studies no 8 and W.H.O Monograph Series no 8 Rome and Geneva 1952. See Lancet, 1952 ii, 1070

[5] Syndrome Policarencial Infantil (Kwashiorkor) and its Prevention in Central America F.A.O Nutritional Studies no 13 Rome 1954 Obtainable from H.M Stationery Office Pp 81 5s

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### University of Oxford

On Feb 26 the degree of D.M. was conferred on J F D Frazer and A L. Turnbull

### University of Cambridge

Prof Dorothy Russell has been elected into a supernumerary fellowship of Girton College

### University of London

Dr E A. Wright experimental pathologist at the Medical Research Council's experimental radiopathology research unit at Hammersmith Hospital has been appointed to the university readership in pathology at St. Mary's Hospital Medical School

### University of Aberdeen

At the July graduation the honorary degree of LL.D will be conferred on Prof John Cruickshank, who retired from the chair of bacteriology last year

### University of Dublin

The honorary degree of SC.D is to be conferred on Prof L J Witts.

### Royal College of Surgeons of England

On Tuesday April 5 at 5 P.M at the college, Lincoln's Inn Fields London W C.2 Mr V E Negus will give the Lister Oration on the Comparative Anatomy and Physiology of the Respiratory Tract in Relation to Clinical Problems.

### Pharmaceutical Society of Great Britain

At a meeting of this society to be held at 17 Bloomsbury Square London W C 1 on Monday March 14, at 7.30 P.M., Mr G Brownlee D.SC reader in pharmacology in the University of London and editor of the *Journal of Pharmacy and Pharmacology* is to speak on the Attack on the Tubercle Bacillus.

### Chemical Aspects of Thyrotoxicosis

A discussion on this subject will be held under the auspices of the fine chemical group of the Society of Chemical Industry at the Westminster Medical School on Friday, March 18, at 6 P.M Prof N F Maclagan will be in the chair and the speakers will include Dr A Lawson Dr J H. Wilkinson and Dr I C Gilliland.

### International Society of Surgery

The sixteenth congress of this society will be held in Copenhagen from July 24 to 31 under the presidency of Prof Evarts A. Graham (St Louis) The programme includes discussions on the Risks of Surgical Operations and on Hepatectomy Further particulars may be had from Mr H. W S Wright 9 Weymouth Street London W 1

### Travelling Fellowships

The Medical Research Council invite applications for four Eli Lilly and one Lederle travelling fellowships

These fellowships are intended for graduates resident in this country with some training in research work who are likely to profit by a period of work at a centre in the United States before taking up positions for higher teaching or research in the United Kingdom. They will normally carry a maintenance allowance at the rate of $2700 per annum for a single fellow and $3900 per annum for a married fellow Provision will also be made for travelling and other expenses Forms of application may be had from the secretary of the council, 38 Old Queen Street, Westminster S W 1 with whom applications must be lodged not later than March 18.

### Decision in Samuels's Cancer Therapy Case

The Netherlands high court has upheld the judgment of the Amsterdam court of justice in the case of Dr J Samuels about whom a complaint was received from the medical inspector of health, accusing him of undermining confidence in the medical profession A medical court in Amsterdam accepted the validity of the complaint and withdrew by a judgment pronounced on March 17 1953 Dr Samuels's authority to act as a medical practitioner After the decision of the high court the Amsterdam court of justice ordered its sentence to be published in the *Nederlandsch Tijdschrift voor Geneeskunde* The decision of the court is based on a report to the Dutch minister of health by Dr J J Brutel de la Rivière on the value of Samuels's short wave ray treatment of cancer

### Polar Medal

The Queen has conferred this medal on Dr G W Marsh, who was base leader and medical officer at Hope Bay in 1952–53 during the Falkland Islands Dependencies survey

### Royal Statistical Society

*Study Circle on Medical Statistics* —On Tuesday, March 29, at 6 P M, at the Westminster Medical School, Horseferry Road, London, S W 1, Dr C J Donelan, Dr K W Cross, and Prof R M Titmuss will speak on Hospital Statistics

### Brompton Hospital Association

A dinner of this association will be held on Friday, April 15, at the Waldorf Hotel, Aldwych, London, W C 2, Dr G E Beaumont will preside Further particulars may be had from the hon secretary, Brompton Hospital, S W 3

### Sanitary Inspectors' Pay

On March 7 the Industrial Disputes Tribunal announced new salary scales for sanitary inspectors, fixing a minimum of £540 a year (instead of £490) for those with statutory qualifications The new rates will come into force on April 1

### Universities Federation for Animal Welfare

The federation's Easter congress will be held at the University of Reading from April 1 to 4 Further details may be had from Miss M P Williams, UFAW, 7a, Lamb's Conduit Passage, London, W C 1

### Christian Medical Fellowship

At a meeting of the fellowship on Thursday, March 17, at 8 15 P M, at the Royal Empire Society, Northumberland Avenue, London, W C 2, Mr S Aldis will speak on the Extent of Medical Responsibility

### Airborne Medical Society

The annual dinner of this society will be held at the Royal College of Surgeons, Lincoln's Inn Fields, London, W C 2, on Friday, March 18, at 7 30 P M Particulars may be had from the secretary, Dr J S Binning, medical department, Marylebone Station, N W 1

### British Association of Sport and Medicine

After the annual general meeting of this association, which is to be held at 5 P M on Monday, March 21, at St Mary's Hospital Medical School, London, W 2, Dr Roger Bannister will speak on Athletics and Physiology Anyone who is not a member but who wishes to attend should write to Dr D J Cussen, Medical Department, St Helen's Court, E C 3

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*Orotracheal Connection with Minimal Resistance* —In the note by Dr John Bullough which we published on Jan 29, under the heading of New Inventions, it should have been stated that a full account of this device and its clinical applications, including a comparison with standard apparatus available in this country, will shortly appear in *Anæsthesia*

## Appointments

BALL, J D M B Lond, M R C P physician in charge of the Miners' Chest Diseases Treatment Centre Llandough Hospital Cardiff

DAVIES, B N M B Wales whole time asst chest physician (S H M O) Llanelly area

GUILMANT M. V, M R C S whole time senior casualty officer Royal Halifax Infirmary

LAIRD R. M M.B Belf F R.C S asst surgeon east Antrim H M C

LASK SAMUEL, M D Leeds M R C O G member of the general practitioner staff Queen Victoria Hospital, Hanwell

LLOYD ROBERTS G C M B Camb F R C S part time orthopædic surgeon, The Hospital for Sick Children, Great Ormond Street, London

MCINROY, R A M.B St And D T M & H part time consultant in pathology Bradford area

MILLER S J H M D Aberd, F R.C.S D O.M.S ophthalmic surgeon The National Hospital Queen Square, London

MUIR I F K., M B E M B Lond, F R.C.S plastic surgeon West Middlesex Hospital, Isleworth

ROBERTS K J M R C.S D OBST asst school M O Hanley Stoke-on Trent

**South Western Regional Hospital Board**

FULLER, ANGELA D M B Camb D C.H pædiatric registrar Southmead Hospital Bristol

GALLAGHER, M. J, M B Queensland, F R C.S orthopædic registrar Princess Elizabeth Orthopædic Hospital Exeter

JOLLY G F M B Camb D OBST registrar in obstetrics and gynæcology Southmead Hospital

KNUTZEN J S, M B Cape Town E.N T registrar, Bath group of hospitals

WEST MARY F M B Lond anæsthetic registrar Southmead Hospital

## Diary of the Week

MARCH 13 TO 19

### Tuesday, 15th

INSTITUTE OF DERMATOLOGY, St John's Hospital Lisle Str W C 2
5 30 P M Dr A D Porter Actinic Eruptions

SOUTH WEST LONDON MEDICAL SOCIETY
8 30 P M (Bolingbroke Hospital Wandsworth Common S.W 1) Mr E G Muir Abdominal Emergencies

MANCHESTER MEDICAL SOCIETY
4 30 P.M (Medical School) Sir Eardley Holland The Princ Charlotte of Wales—a Triple Obstetric Tragedy (Univers lecture)

### Wednesday, 16th

UNIVERSITY OF LONDON
5 30 P M (Westminster Medical School Horseferry Ro S W 1) Academician W A Engelhardt Mecha chemistry of Muscle (Second of two lectures)

ROYAL SOCIETY OF MEDICINE 1, Wimpole Street W 1
5 P M *Comparative Medicine and Pathology* Dr J Christ Slim (Copenhagen), Prof C. P Beattie Dr I A Cathie Toxoplasmosis

INSTITUTE OF DERMATOLOGY
5 30 P M Dr J O Oliver Allergy and Immunity in S Diseases

INSTITUTE OF DISEASES OF THE CHEST Brompton S W 3
5 P M Dr R W Riddell Bacterial Resistance in the Treatm of Tuberculosis

HYPNOTHERAPY GROUP
8 P M (1, Wimpole Street W 1) Dr J A Hadfield T Place of Suggestion in Analytic Treatment

ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE, 28 Portl Place W 1
3 30 P M Dr J Greenwood Wilson Housing and Health

MIDLAND MEDICAL SOCIETY
8 15 P M (Birmingham Medical Institute, 154, Great Cha Street) Prof J H Dible: Peripheral Vascular Disord

ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASGOW, 2 St Vincent Street, Glasgow C 2
5 P.M Prof Robert McWhirter Breast Cancer

### Thursday, 17th

ROYAL COLLEGE OF PHYSICIANS OF LONDON Pall Mall East S.
5 P.M Prof W Melville Arnott Order and Disorder in monary Function (First of two Oliver Sharpey lectu

UNIVERSITY OF LONDON
5 P M (University College Hospital Medical School W.C Miss Honor Fell D.SC, F R S Response of Organ Culture to Environmental Influences

ROYAL ARMY MEDICAL COLLEGE Millbank, S W 1
5 P M Lieut Colonel H Neville Stafford Coroner's Pra and Procedure

BRITISH INSTITUTE OF RADIOLOGY 32, Welbeck Street W 1
8 P M Dr G E Flatman Mr R E Ellis Use of Conver Beam X ray Therapy at the Middlesex Hospital. K Y Ortan Rotation Therapy with the 2 MeV der Graaf Generator in Sheffield

WEST LONDON MEDICO CHIRURGICAL SOCIETY
7 P M (Rembrandt Hotel Thurloe Place, S W 7) Sir Ju Charles Counting the Cost

NUFFIELD ORTHOPÆDIC CENTRE, Wingfield Morris Orthopa Hospital, Oxford
8 30 P.M Prof O Scaglietti (Florence) Congenital Disloca of the Hip

NORTH WESTERN TUBERCULOSIS SOCIETY
5 P.M (Manchester Royal Infirmary) Dr L F Hought Corticotrophin in the Treatment of Pulmonary Tube losis

MANCHESTER MEDICAL SOCIETY
8 P M (University staff house) *Anæsthetics* Dr Geoff Organe Polypharmacy and Balanced Anæsthesia.

### Friday, 18th

POSTGRADUATE MEDICAL SCHOOL OF LONDON Ducane Road, W
2 P M Mr R S Murley Carcinoma of the Female Breas
4 P M Dr R A J Asher Medical Uses of Hypnotism

ROYAL SOCIETY OF MEDICINE
8 15 P.M *Radiology and General Practice* Dr David Bro Dr J S Fulton Radiotherapy from the Gene Practitioner's Point of View

FACULTY OF RADIOLOGISTS
5 P.M (Royal College of Surgeons of England Lincoln's I Fields London W C 2) *Radiotherapy* Mr G W Blomfiel An Evaluation of the Clinical Results in 2 million V X ray Therapy

ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASGOW
5 P M. Dr J H Hutchison New Diseases in Pædiatrics.

### Saturday, 19th

BIOCHEMICAL SOCIETY
10 45 A.M (University College Gower Street W C 1) Scienti papers

FELLOWSHIP OF POSTGRADUATE MEDICINE
10 A M (St Stephen's Hospital Fulham Road, S W 10) Pr A L Banks Social and Economic Aspects of t Rheumatic Diseases (Opening lecture of week course in the rheumatic diseases)

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The Proceedings of the World Congress of Doctors for the Stu of Present day Living Conditions held in Vienna in May 195 have now been published Copies (10*s* 6*d*) can be had from t Caversham Centre 25 Caversham Road London N W 3

# INSTINCT AND THE NURSING COUPLE

MAVIS GUNTHER
M.A M.D Camb
*From the Obstetric Hospital University College Hospital London*

ALTHOUGH survival of the human race through the processes of evolution must have depended on successful feeding from the breast there can be no doubt in the minds of those taking care of modern Western European and American women during the puerperium that instinct does not inform the mother how to feed her first baby Many mothers are aware of this failure which if they think about it is all the more remarkable since labour which is part of the same job is most effectively compulsive The mothers sometimes secretly believe that they must lack innate maternal feeling and they are distressed by this apparent inadequacy

Middlemore (1941) has pointed out that some chimpanzees when delivered in captivity have also not known what to do with their newborn babies In fact the first two chimpanzees born in captivity (Reid Blair 1920) died of starvation without ever getting on the breast Two others were successfully fed after the keepers had taught the mothers how to suckle, but one chimpanzee refused to have anything to do with her infant (Budd et al. 1943 Wyatt and Vevers 1935) When a female chimpanzee cannot rear her young without having a human male to teach her instinct in the mother may indeed be said to have failed. One chimpanzee Sally, who knew how to feed her infant had unlike the others come to captivity relatively late in life, at about the age of 3 years (roughly equivalent to 6 or 7 in humans)

One explanation of this failure could be that in primates and man mimicry takes the place of instinct Presumably the chimpanzee Sally had lived in a colony and seen suckling practised In humans the small size of present-day families and the conventions of modesty combined with housing which allows privacy have ensured that most women do not as children watch a baby being suckled In London it is rare for more than one in ten primigravidæ to have seen an infant feed from the breast—far less to have an easy familiarity with the process from frequent watching

Whatever the explanation of failure of this instinct in women there is no doubt that feeding from the breast is more likely to succeed if the process is understood

### *The Baby's Part*

In the animal kingdom the initiative is often taken by the neonate who may have the mobility and the instinctive compulsion which enable it to find the nipple and the mother's part is to be completely inert For instance the piglet at birth is compelled presumably by smell, to scramble round or over its mother's hind legs until it reaches an unseen nipple while the mother lies still. The human mother must take the active part which brings the two *together*, but, even if she puts the baby near the breast, the baby though awake and apparently hungry may fail to feed

When large numbers of babies are watched in their first attempts to feed various patterns of behaviour can be seen In the first place immediately *after birth and* later the baby may make sucking and kissing movements of the lips and mouth open his mouth asymmetrically and turn his head with or without the stimulus of a touch on the lips This first *activity* appears to be a measure of the baby's state of excitation and though the movements are coördinated apparently purposive and clearly suggestive to the mother, they do not necessarily lead to *feeding* even if the baby is held near the breast As the baby becomes sleepy these movements may subside without the satisfaction of nourishment.

Where feeding is easy the next phase may follow without being recognised but where there is slight difficulty there is often one point, clearly recognisable to the mother and her attendant, when the baby changes in responsiveness This change occurs when the baby first experiences the filling of his mouth right to the palate and the dorsum of the tongue with a nipple or a nipple substitute of the right shape The full action of the jaws tongue and cheeks is evoked and from then on the baby can almost put himself on the breast It has been *noticed* that where the *mother's* breasts were sufficiently well formed for the baby to hold the nipple in the lips but not protractile enough to evoke the full feeding response the baby was apathetic. He settled on the nipple quietly and was not interested The nurses described him as lazy or like a premature baby in behaviour The pædiatricians *looked for infection*

### *Nipple shape as Sign Stimulus?*

The concepts of instinctive behaviour in animals lately put forward by Lorenz (1952), Tinbergen (1951) and their co workers have their counterpart in the behaviour of the newborn baby A newly born or newly hatched *animal does not react to all* the changes which its sense organs can perceive but only *to a few of them* The stimuli operate within a limited perceptual world (Tinbergen 1951) The limitation may be to one type of sense and within that to limited qualities and patterns of stimuli which in a specific way evoke responses which are more elaborate than reflexes *If the essential* quality and pattern of stimuli is presented by an artifice the same behaviour may be evoked and the animal then appears to have made a mistake Classical examples of this are the gosling's attachment to its first living companion, even if human (Lorenz 1952) *and the* young herring gull's attempt to feed from a red spot without a head attached to it rather than from a herring gull's bill and head without a red spot (Tinbergen 1951) Manifestations of instinctive behaviour have been found to be evoked by a limited and definable stimulus called a sign stimulus, which releases an innate mechanism within the *animal* The consistency of the response its apparent purposiveness and its degree of coördination even when evoked without previous experience qualify the action to be called instinctive

A baby is led to suck not by sight hearing smell, or taste but by tactile stimuli alone Two forms can be distinguished ; the touch on the circumoral area which *is more rousing* than touch in other parts of the body but which at first has no *specific effect and* touch within the mouth with an article whether nipple bottle *teat* or adult finger which by its shape modifies the baby's responsiveness lastingly The specificity of the stimulus and the lasting *modification* which it effects suggest that this is a sign stimulus working *on an innate* release mechanism The non specific early activity of sucking mouth movement, and head turning is thought to be a *form of* innate automatism

In animals *some forms of instinctive* behaviour may be evoked only during a limited and *appropriate* phase of the animal's life In the neonate the sign stimulus—the filling of the mouth with a specific shape—must occur within *four* or five days after birth or the full effect of the response may be *lost*

## Investigation

If the physical shape of the nipple is the sign stimulus of instinctive activity in feeding, it should be possible from the mother's *breast-shape to* predict the baby's feeding behaviour To test this hypothesis I *investigated* the breast shape of 160 women

### *Method of Assessment*

When a baby takes the breast he draws the nipple to the back of his mouth, and the gums lips, and tongue

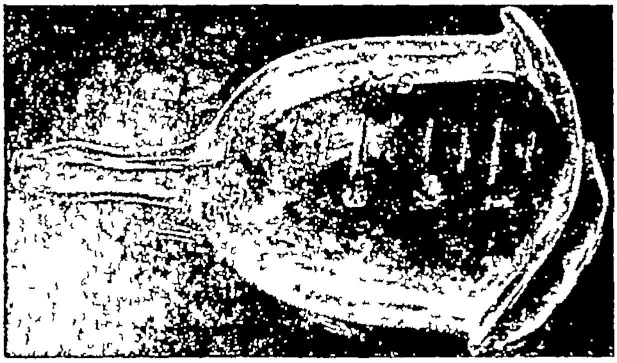

Fig 1—Instrument for measuring protractility of nipple

hold and work on the yielding tissues underneath the areola and behind the nipple A well-formed nipple enables a baby to take a breast more easily than one which has no substance, but the shape of the nipple is secondary in importance to the length which the tissues behind the nipple offer to the baby's mouth For the tissues to be accessible the nipple must be not too large to enter past the baby's bite, and the tissues when drawn forward must be able to pass the gums

In designing an instrument to measure the protractility of the nipple and the tissues behind it, the first step was to measure the distance between the gums of a number of babies This was done by touching their mouths with sterile glass-plates and measuring through the glass while the babies tried to suck the plates 2 cm was found to be a usual measurement

A glass instrument was then made somewhat resembling a mouth in shape—a flattened tube with internal diameters of 4 and 2 cm The open end was curved like jaws, the other was connected to a source of suction and a manometer The instrument was graduated in centimeters from the jaw end (fig 1) For use, the open end was put over the nipple and over as much areola as could be put into it, a suction of 60 mm Hg was applied, and the distance which the nipple reached down the tube was recorded

*Results*

The distribution of the patients in the groups of measurement is given in table I

TABLE I—PROTRACTILITY OF BREAST IN 150 WOMEN

| — | Protractility (cm) | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | 2 | 2 25 | 2 5 | 2 75 | 3 0 | 3 25 | 3 5 | 3 75 |
| Primiparæ | 4 | 10 | 41 | 33 | 18 | 0 | 0 | 0 |
| Multiparæ | 0 | 0 | 8 | 9 | 18 | 6 | 2 | 1 |

It will be noted that parity improves the shape of the breast Of the 87 women offering a length of 2 75 cm or more, 7 failed to feed their babies (2 because the mothers were unwilling, 2 because the mothers were ill, and 1 because of true prematurity), and only 2 of the failures were connected with breast shape The success of the 63 women with short accessible hold is given in table II

Among the 16 "unsuccessful" mothers with measurements of 2 5 cm or less, 3 failures were unrelated to breast shape (1 unwilling mother, 1 ill baby, 1 truly premature baby) 2 (2 cm length) failed because the baby was unable to take the breast 3 of the babies whose mothers' measurements were 2 5 cm or less, and 1 whose mother had a larger measurement, failed because they fought at the breast But 8 failed because of their apathy 5 of the 8 were given no substitute for oral stimulation Usually if a baby will not feed by the third day supplementary food is given in a way which provides a sign stimulus—by bottle Each of the 5 had been paired at birth with another baby, chosen because the mother had an adequate protractility length The 5 pairs of babies received all extra feeds in the first five days of life from a spoon The 5 whose mothers' breasts were well formed fed and developed normally, but all the other 5 remained apathetic feeders for at least four weeks The nursery staff were kept in ignorance of the nature of the investigation while it was in progress and are believed to have treated the babies equally Many other babies showed an apathetic response for the first two or three days, but soon became eager takers when their positions at the breast were improved and they obtained full oral stimulation

Confirmation of the relation between the vigour of the baby and oral stimulation came from twins whose mother's breasts were sufficiently protractile The larger, a boy weighing 7 lb, was apathetic while the smaller girl was vigorous The boy had a much smaller mouth and never drew his mother's exceptionally large nipples to the back of his mouth

I suggest, therefore, that an adequately shaped breast, presenting a nipple as a knob with yielding tissues beneath the areola, acts as a sign stimulus to the baby Where this fails, the critical time for its reception may pass, and a more than fleeting apathy results A bottle teat may take the place of the natural sign stimulus and may even serve better than a poorly shaped one

Ethnologists have found some artificial sign stimuli to be more effective than the natural ones For instance, an oyster-catcher, presented with her own eggs and with wooden ones of twice the size, sits on the wooden ones. A bottle-teat may similarly be a supernormal sign stimulus

TABLE II—FEEDING BY 63 WOMEN WITH SHORT ACCESSIBLE HOLD

| — | Protractility (cm) | | | | | |
|---|---|---|---|---|---|---|
| | 2 0 | | 2 25 | | 2 5 | |
| | Primip | Multip | Primip | Multip | Primip | Multip |
| Successful | 1 | 0 | 4 | 0 | 34 | 8 |
| Unsuccessful | 3 | 0 | 6 | 0 | 7 | 0 |

Primip = primipara Multip = multiparæ

*Apathetic Response*

Breasts alter in shape in the first days of lactation. This alteration was at a minimum in this investigation, because the mothers received minute doses of œstrogens after delivery and did not develop engorgement Where the baby failed to keep up with secretion, milk was removed with a milking machine which did not disimprove the shape of the breast Variation in shape seemed to be a minor factor, no greater than those introduced by variations in the baby's posture at a feed

When the baby would not feed the mother became discouraged and sometimes she gave up quickly

A distinction should be made here between the baby who responds to the bottle though his innate mechanism was not released by the breast, and the baby who is not really interested in the bottle when he ultimately gets it This second type have been classified as lastingly apathetic It seemed that those whose release mechanism had been activated by a bottle teat where it was supernormal to the mother's breast soon used a different mouth mannerism in expectation of the bottle teat Their lips were more O shaped and the tongue tended to go up This is often noticed by midwives The mannerism makes breast feeding harder to achieve Nipple shields and complementary bottle-feeds will have this effect, despite good position at the breast, if the available hold is definitely short Here the mother gives up, not only because of her own rejection, but because of the success of the bottle If feeding is going to be possible,

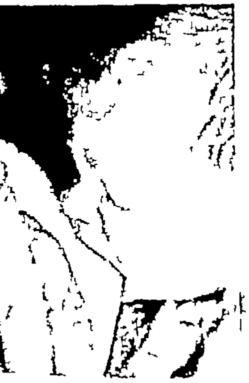

Fig. 2—Correct position of lip

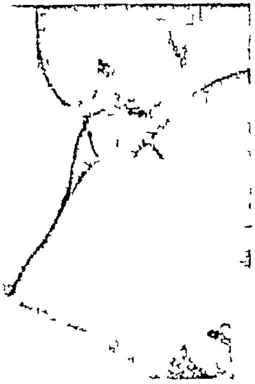

Fig 3—Faulty position of lip.

tle-teats should not be given to these babies In
her type of apathy, secretion may be reduced by the
other s distress.

Another form of behaviour at the breast which caused
ture in 4 cases in the present investigation is for the
by to fight and press himself away from the mother
hen the sequence of events is watched it is found
at when these babies have been put to the breast the
way has been obstructed—sometimes by the breast
by nasal obstruction but most commonly by the
by s upper lip rising up and covering the nostrils
mally a baby who has received one or more full oral
small curls his upper lip down (fig 2), keeping the
way clear but in some with faulty position and in
any where the wide angle of the breast makes the
ld short and insecure the upper lip curls up (fig 3)
t has been maintained that newborn babies are not
ally conditioned; but this fighting response typical
f an anoxic baby can be established by two or three
odes—after which it is seen before the baby even
hes the breast If the physical satisfaction is provided
y a bottle teat and the child while tranquil is turned
wards the mother the breast can be quickly substituted
r the teat and the baby usually learns to feed normally
fter two or three successful feeds This conflict between
e primary urges to breathe and to feed is a common
st neurosis which can easily be resolved once it is
membed

## Discussion

The feeding behaviour of nurslings was described by
iddlemore (1941) with delightful accuracy She con
dered many possible reasons for the existence of types
f behaviour and suggested that babies were born into
eir categories and that the mother s handling con
ibuted to their make-up All the observations which
e made can take their place in the types of behaviour
scribed in this investigation but viewed from the
ferent standpoint their interpretation is different

Middlemore says The active satisfied babies estab-
shed the sucking reflex and rhythm quickly and
owed their pleasure by seeking the nipple when it
as withdrawn ' This describes babies after full oral
tisfaction Under the heading sleepy satisfied suck
ers," she mentions that the gently sucking child does
t draw the nipple deeply into his mouth—not far
ough to activate the chain of the sucking reflex
They did not move much or cry at the breast It is
rd to distinguish these babies, and the simply inert
who were like premature children only in dullness and
k of vigour,' from those I have classed as apathetic
The " excited ineffective sucklings scrambled about the
breast their desire for the nipple was evidently strong but contact with the breast was unpleasant " fits exactly the baby I have described as fighting ' the breast Middlemore mentioned that these babies were often clumsily handled That is almost always so but the clumsiness seems to be the result and not the cause of the baby s behaviour

There has long been a controversy (Engelmann and Hamburger 1927 Reiprich 1929) about the time when a baby should first go to the breast Hippocrates Harvey (1766) and Erasmus Darwin (1801) have pointed out that normal babies will suck at birth and it has often been said that if a child is put straight to the breast after birth feeding presents no difficulties This was open to the interpretation that a midwife would only trouble the mother to suckle where the conformity of the breasts would make feeding easy

If as is now suspected the vigour of the response in the baby fades if full stimulation has not been experienced in the first days, there seems reason to accept the wakefulness of the baby immediately after birth as the time for his first feed Newborn calves are fully active soon after birth and then tend to be sleepy for ten hours or more and this sleepiness seems to come to babies too There may then be only a few opportunities for the baby to take the breast for even a well shaped breast may become difficult if engorgement arises and the chance may be missed Anxiety is sometimes expressed about the danger of vomiting if babies are fed soon after birth This point needs further investigation. It is remarkable however, that a baby who has been induced to swallow what he does not like will probably spew it back, whereas if a pleasant taste is added the unpleasant material is not returned Agreeable tasting colostrum probably acts as a confirming stimulus and may have the additional effect of sending the stomach contents along its proper path

I have in this paper laid emphasis on the importance of length of hold offered by the yielding tissues of the breast behind the nipple Measurement has confirmed that when a breast is assessed early in pregnancy the criterion of adequacy should not merely be a feeling that one could get a baby to take that nipple but whether the breast when compressed by the finger and thumb laid on the margins of the areola will offer a hold roughly as long as a bottle teat after passing a 2-cm gap Where it does not the mother should be given treatment with shells designed by Waller (1946) who estimated that 40% of British primiparæ need this help Poorly shaped breasts are common in fair haired Europeans, especially among the redhaired and I have not seen them in Negroes though they have been noticed in Africa by Williams (1955)

I hope that this description of how a baby s instinctive action of feeding is aroused will draw attention to the strength of the instinctive response If this is recognised, the aim of antenatal breast care becomes clearer and the mother has a better chance of suckling her baby successfully

Breast feeding is often the first—and a very important—form of mother and child relationship When a mother is very anxious to feed her child and he refuses and fights she is profoundly depressed She may be found weeping before each feed and her delight in her child may be completely taken away by her misery The mother of the apathetic baby has an urge to chivy her baby and may do so for weeks The mother of one of the apathetic babies of this investigation , rt that soon after leaving hospital she had to a clinic because the baby was such a poor feeder The nurse in charge, with every good intention, devoted herself for three days to rousing the baby, tweaking, pinching, and slapping it during all feeds She recommended that the father should do the same for as long as necessary One can imagine that the mother's despair at the child's poor urge to feed had already provided a basis for an unhappy relation between father, mother, and child If these two types of failure in suckling technique can be avoided a positive step will have been taken towards a secure relationship

But the other side of the picture should not be forgotten A trick should not be used to deprive a nursing couple of the time of wooing, and there is no need to tell a mother that she will not know how to feed her baby, nor is there need to imply by gesture that a third person's aid is necessary If the mother's nipples are sufficiently protractile, and if she sits comfortably in a good position, the help given need not intrude on the mother's tenderness towards her baby

### Summary

Instinct does not necessarily inform a mother how to feed her baby

The baby's part is an instinctive response comparable to instinctive behaviour described in animals The nipple, and the protractile tissues behind it, when put far into the baby's mouth act as "sign stimuli" The degree of protractility was found to be related to success in feeding from the breast Where the protractility was deficient, the baby was likely to be unresponsive

A baby may fight at the breast This behaviour is thought to be a conditioned response arising from difficulty in breathing during a few feeds

It is a pleasure to thank Prof W C W Nixon and Dr R E Bonham Carter, in whose departments this work was carried out, and also Sisters M Curtis, D Lyon, and M Seligman for their unstinted help

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# TREATMENT OF RHEUMATOID ARTHRITIS BY PROLONGED STIMULATION OF THE ADRENAL CORTEX

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IT has been generally assumed that for rheumatoid arthritis cortisone therapy and corticotrophin therapy amount to the same thing There have been accounts of patients treated for prolonged periods with known amounts of cortisone acetate, but there has been no account of a group of patients treated for a prolonged period with known amounts of adrenal stimulation This paper reports such a group

Theoretically there may well be qualitative differences between treatment with cortisone acetate and by adrenal stimulation Cortisone acetate therapy involves the suppression of the adrenal's output not only of hydrocortisone but also of corticosterone and several other steroids secreted in small amounts, including both corticosteroids and 17 ketosteroids That only the hydrocortisone plays a part in metabolism is an assumption

Corticotrophin, on the other hand, stimulates the secretion of all these substances and may have, in addition, effects on metabolism that are independent of the adrenal glands If corticotrophin was a pure non antigenic hormone that could be standardised in such a way that a given intramuscular dose would provide a known degree of adrenal steroidogenesis, it would be easy to assess the therapeutic value of different degrees of adrenal stimulation As it is, we find that the adrenal response to a given intramuscular dose of corticotrophin varies from patient to patient, and, in any one patient, from time to time This being so, it is essential to make repeated assessments of the corticosteroid output of the adrenal glands to study the effect of any level of adrenal stimulation over a prolonged period In this study the assay of urinary 17 ketogenic steroids (Norymberski et al 1953) has been used to this end

### Choice of Patients

The patients we chose for both corticotrophin treatment and cortisone treatment were incapacitated by active and progressive rheumatoid arthritis and had not improved at all after much conservative therapy Their allocation to treatment with corticotrophin or with cortisone acetate was determined almost entirely by the availability of these preparations, and so it will be reasonable to compare the corticotrophin treated group with the group receiving long-term cortisone acetate therapy previously reported (West and Newns 1953)

### Dosage

Various brands of long-acting corticotrophin were used, and such doses were given as would lead to a daily urinary output of 15–40 mg of 17 ketogenic steroids, the level aimed at depending on the severity of the rheumatoid arthritis at the time A daily output of 15 mg of 17-ketogenic steroids is usually too little to have any effect, and an output of 40 mg of 17-ketogenic steroids is usually too high to be maintained for many weeks without causing hypertension The doses of corticotrophin found necessary were $7^1/_2$–40 units given daily by intramuscular injection The unit contains a third of a U S P unit of corticotrophin, since the makers assume that in the long acting form the corticotrophin will be three times as potent as in the rapidly absorbed aqueous form

With twelve hourly injections of long-acting corticotrophin the daily urinary output of 17 ketogenic steroids may progressively rise to well over 100 mg a day, whereas the highest output that we have observed in the twenty four hours following a severe surgical operation has only been 55 mg To control the level of adrenal stimulation we assay twenty-four hour specimens of urine every five to seven days until a suitable maintenance level has been found, and subsequently not less than monthly

### The Patients

11 patients were treated continuously for from one to two years Of those who stopped receiving adrenal stimulation before a year was completed none did so because the therapy was ineffective or inadequate and only two stopped because of complications In each case excessive adrenal stimulation was responsible This could have been avoided One patient had scleroderma as well as rheumatoid arthritis There were 6 males aged 16–51 (average 41) and 5 females aged 41–69 (average 50)

### Duration of Disease at Start of Corticotrophin Therapy

In the males the disease had lasted from 3 months to 13 years (average 4 7 years) and in the females from 2 to 20 years (average 6 5 years) In only 1 patient was disease of short duration he was aged 14 had had ere rheumatoid arthritis for 3 months, and his fever not responded to eight weeks' salicylate therapy

### Duration of Corticotrophin Treatment

he males were treated for 12–17 (average 15) months the females for 12–24 (average 17) months

### Findings

*hrocyte-sedimentation Rate*

t the start of corticotrophin treatment the average throcyte sedimentation rate (E.S.R.) was 38 mm in hr (Wintrobe) and at the end of treatment 10 mm 1st hr The changes in the 11 cases were as follows

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| 35 | 50 | [illegible] | 0 | 37 | 13 | 32 | 62 | 57 | 43 | 51 |
| ↓ | ↓ | ↓ | ↓ | ↓ | ↓ | ↓ | ↓ | ↓ | ↓ | ↓ |
| 8 | 7 | 20 | 9 | 20 | [illegible] | 36* | 40* | 11 | 23 | 30 |

* Adrenal stimulation was slight at this time

*emoglobin*

At the start of corticotrophin treatment the average ount of Hb was 12 3 g per 100 ml., and at the end of atment 13 3 g per 100 ml The individual changes re as follows:

*Males*

| | | | | | |
|---|---|---|---|---|---|
| 12·6 | 10 8 | 16 5 | 15 5 | 14 5 | 12 3 |
| ↓ | ↓ | ↓ | ↓ | ↓ | ↓ |
| 15 1 | 15 8 | 16 4 | 14 4 | 15 1 | 12 6 |

*Females*

| | | | | |
|---|---|---|---|---|
| 13 7 | 10 5 | 8 7 | 9 7 | 11 0 |
| ↓ | ↓ | ↓ | ↓ | ↓ |
| 13·0 | 8 7 | 9 3† | 12 6 | 13 7 |

This patient's anæmia was due we think to malnutrition For family reasons she had to stop the injections after 18 months, and change to 50 mg. of cortisone She has been fed properly from that time, and her Hb is now 12 g per 100 ml.

This patient's Hb increased to 12 g per 100 ml. but has decreased since coincidentally with a gradual failure of H.P Acthar Gel to stimulate her adrenals.

*ite Cells*

At the start of corticotrophin treatment the average ite-cell count was 8600 (range 5410–10 400) per c.mm., d at the end 10 900 (range 4900–16,000) per c mm

*nsophils*

When adrenal stimulation was excessive the eosino hil-counts were usually low At the levels of adrenal mulation we used the counts were meaningless although taken at the same time of day each time)

*lasma*

Monthly estimations of plasma proteins albumin/ bulin ratio plasma fibrinogen and plasma-cholesterol re made for three years in all our patients treated with her corticotrophin or cortisone We have now given em up as a waste of time The serum-cholesterol levels ve not tended to rise The plasma protein levels have turned to normal in the few cases starting with a ss abnormality and have subsequently fluctuated thin roughly normal limits in quite an erratic manner

*eight*

At the start of corticotrophin treatment the patients ighed 77–161 (average 130) lb and at the end 89–169 verage 147) lb

*lood-pressure*

At the start of treatment the blood pressure was 15–180/70–100 (average 127/77) mm Hg and at the end 15–180/70–100 (average 136/84) mm Hg

*rength of Grip*

This was tested with a sphygmomanometer cuff t the start of treatment the strength in the right hand s 30–140 (average 88) mm Hg and in the left hand 110 (average 79) mm Hg and at the end 60–200 + rage 174) mm Hg in the right hand and 40–200 + verage 171) mm Hg in the left hand

*hysical Ability*

This was graded as described by the joint committee of the Medical Research Council and Nuffield Foundation (1954)

Grade 1: fully employed or employable in usual work and able to undertake normal physical recreation.

Grade 2 doing light or part-time work and only limited physical recreation (for housewives all except the heaviest housework)

Grade 3: not employed and unemployable no physical recreation (for housewives only light housework and limited shopping)

Grade 4 confined to house or to wheeled chair but able to look after self in essentials of life (hospital patients confined to bed)

Grade 5: completely bedridden

At the start of corticotrophin treatment the average grade of physical ability was 3 2, and at the end 2 1 This assessment can easily be affected by wishful thinking It is true that every patient felt better in himself or herself and could do more physically The patients were in no two minds about this.

*Radiological Evidence*

The comparison of radiographs before and at the time of review was difficult owing to differences in technique and in the type of films used Nevertheless the following conclusions were reached:

(1) In only 2 cases was there evidence of an extension of bone erosion (a very minor increase) No new erosions were observed

(2) In *no* case was there definite evidence of increased osteoporosis.

(3) In 3 cases the bone density appeared to have improved, but the films were not comparable (allowance had been made for this)

(4) In 1 case the density of the bones of the hands had much improved.

(5) Multiple deposits—calcinosis circumscripta—about the fingers of the patient with scleroderma had almost completely disappeared

(6) In 1 case there was radiological evidence of a rapid increase in bone erosions in 4 months before treatment Since treatment no new erosions have appeared and the edges of existing erosions appear to have hardened.

## COMPLICATIONS

In 4 patients the blood pressure rose somewhat (diastolic from 90 to 100 mm Hg) During moderate adrenal stimulation (30–40 mg of 17 ketogenic steroids) pigmentation appeared in 2 patients A leucocytosis usually accompanied severe stimulation Osteoporosis of the spine has been reported as a complication of corticotrophin and of cortisone treatment The spines of these patients were not radiographed It is our impression from the literature that excessive adrenal stimulation may have been responsible for the cases reported

### Comparison with Cortisone treated Group

| | *Cortisone acetate* | *Adrenal stimulation* |
|---|---|---|
| Physical ability | 3–2 7 | 3 2–2 1 |
| *Grip* (mm. Hg) | | |
| Right | 150–155 | 88–174 |
| Left | 100–153 | 79–171 |
| E.S.R. (Wintrobe) (mm. in 1st hr ) | 34–29* | 38–10* |
| Hb (g per 100 ml ) | 11 3–12 3 | 12 3–13 3 |
| White cells (thousand per per c.mm.) | 7700–9200 | 9600–10 000 |
| Blood pressure (mm Hg) | 131/79–135/84 | 127/77–136/84 |
| Weight (lb ) | 130–143 | 130–147 |

* These figures need qualification The pre-treatment E.S.R for the cortisone-acetate patients was an average of the readings taken for the six months before therapy began The readings for the corticotrophin treated patients were taken immediately before treatment began and may well have been higher in consequence Further when 22 long term cortisone-acetate patients were transferred to Cortisol (hydrocortisone free alcohol) for three months their average E.S.R. fell further to 27–21 5 mm. in 1st hr (West and Newns 1954 )

*Radiological Findings*

In the cortisone acetate group 16 of 27 patients showed evidence of new bony erosions or of increase in existing erosions The adrenal stimulation group revealed only 2 of 11 with some increase in bony erosion

COMPLICATIONS

The only complications in the adrenal-stimulation group were those mentioned above In the cortisone-acetate group (almost three times the size) there were 5 instances of intestinal hæmorrhage in 3 patients

### Discussion

There seems to be little doubt that, under the conditions of these trials of controlled adrenal stimulation and cortisone acetate therapy for severe rheumatoid arthritis, the former method has produced better results One is forced to the conclusion that adrenal stimulation, at the levels described, has favourably affected the course of rheumatoid arthritis in this particular group of patients—so far

Since this conclusion carries with it important implications, we have gone over the records of these patients with great care and have studied them in graphic form, looking for any evidence that might upset the conclusion The only observation that came to light was that the results might well have been better, in some instances, had the level of adrenal stimulation been adequate (without being excessive) It must be emphasised, of course, that there is no question of patients having been cured, and it must be remembered that the patients are still receiving treatment

The technical disadvantages of corticotrophin treatment lie in the need for daily injections and for urinary assays Our patients have given their own injections (about 10,000) without mishap As regards the assays, these are no more difficult than assays for 17-keto steroids Both disadvantages would be reduced if corticotrophin could be produced with a longer action and with a constant effect when given intramuscularly A further disadvantage not gone into here is the possibility of allergic or anaphylactic reactions in patients given repeated courses of corticotrophin On the credit side is the fact that on withdrawal of corticotrophin therapy the adrenal glands are left active and possibly enlarged, whereas on withdrawal of cortisone treatment they are inactive and possibly smaller

### Conclusions

The study of this small group of rheumatoid patients receiving mild to moderate adrenal stimulation for from one to two years suggests that the maintenance of a daily urinary output of 20–35 mg of 17-ketogenic steroids will favourably influence the course of moderately severe rheumatoid disease In consequence we feel that every effort should be made to extend this therapeutic trial and to find a more satisfactory adrenal stimulant for long term use than the present preparations of corticotrophin

The preparations of long acting corticotrophin were supplied by the joint committee of the Medical Research Council and the Nuffield Foundation for the trial of cortisone, corticotrophin, and other therapeutic measures in the treatment of chronic rheumatic diseases

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"Democracy has been described as being like the perfect wife—lovely, but not fast "—Mr J R H Hutchison, *Hansard*, March 1, 1955, col 2014

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# INTRARENAL PRESSURE IN EXPERIMENTAL TUBULAR NECROSIS

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Acute tubular necrosis in man sometimes follows a sudden and sustained reduction in blood volume such as occurs with accidental trauma, surgery, and severe diarrhœa and vomiting, it is a complication of abortion, accidental hæmorrhage, and mismatched blood transfusion, and it can also be caused by the ingestion of certain poisons, such as mercury There is much evidence that all these conditions, whether or not renal failure develops, are associated with renal ischæmia, and it is therefore probable that the tubular necrosis which occasionally takes place is only a reflection of the intensity of this primary ischæmia (Oliver et al 1951), with poisons there is the additional damaging effect of the poison on those tubule cells which are concerned with its secretion into the urine

It has been shown that, once acute renal failure has developed, severe renal ischæmia may persist for several weeks, though the initial stimulus for the ischæmia is no longer present (Bull et al 1950) The cause of this secondary renal ischæmia is not known, but, because kidneys with tubular necrosis are heavier and feel firmer on palpation, and because demonstrable breaches in continuity of some of the nephrons seem to allow free communication between their lumina and the interstitial space, it has been suggested that the ischæmia is due to interstitial œdema (Oliver et al 1951, Oliver 1953, Peters 1945) Decapsulation of the kidneys is a therapeutic extension of this hypothesis

It is impossible to measure the renal interstitial pressure directly, instead, the pressure obtained by inserting a needle into the renal substance has been measured, and this has been called the intrarenal pressure The following experiments were performed to establish what changes take place in the intrarenal pressure when the tubules have recently become necrosed, and what effect decapsulation has, in these circumstances, on this pressure

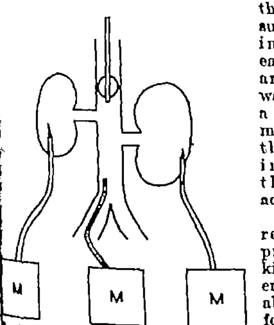
The findings suggest that the renal interstitial pressure in a necrosed kidney is not raised, and that the renal ischæmia is due to vasoconstriction

### Method

Necrosis of the left kidney was produced in dogs by occlusion of the renal artery for three to four and a half hours, the right kidney being used as a control several days later the intrarenal pressure of the two kidneys was measured and compared, in some dogs the pressure was also measured after transient occlusion of the thoracic aorta, and in others before and after decapsulation of the left kidney

The experiments were made on eight dogs, weighing 10–16 kg, anæsthetised with intravenous pentobarbitone The left kidney was exposed through a flank incision, and the renal artery completely occluded with two modified Michel clips (the renal vein was not occluded) After three to four and a half hours the clips were removed and the flank wound was closed Two days later dogs 3–8, and four days later dogs 1 and 2, were again anæsthetised, and then suspended from a horizontal beam Both kidneys were now exposed simultaneously by bilateral flank incisions In dogs 1, 2, 6, and 7 both kidneys were brought out so as to be superficial to the muscle layers In dogs 3, 4, 5, and 8 the kidneys were not disturbed from their normal position in the abdominal cavity, this was obviously a more desirable preparation, at it reduced the available surface into which the needle used for measuring the intrarenal pressure could be inserted.

Continuous and simultaneous measurement of the intrarenal pressure in both the control and the necrotic kidneys was obtained by a technique which has been described previously (Miles and de Wardener 1954) Needles (24 British Standard gauge with an external diameter of 0 56 mm ) filled with heparinised saline solution and joined to capacitance manometers by 'Polythene' tubing 0 5 mm in internal diameter were inserted into either the cortex or the medulla of the renal substance Since no difference was found between the pressure in the medulla and that in the cortex the needles were most often placed in the cortex, when the needle was inserted obliquely to a depth not greater than 0 5 cm. The intrarenal pressure of both kidneys was then observed continuously *for three to eight minutes,* inter mittent or continuous photographic records of the pressure being taken during that time Both needles were then withdrawn and reinserted into different sites and the intrarenal pressure was again measured In this way the intrarenal pressure was measured in 6–12 sites in each kidney The arterial pressure was measured with a mercury manometer via a polythene catheter inserted into the arch of the aorta



1—Technique of obtaining continuous simultaneous measurements of intrarenal pressure of necrosed (left) and control (right) kidneys before, during, and after arterial pressure to both kidneys had been lowered by inflating a soft-rubber balloon in the descending thoracic aorta. Distal arterial pressure was measured via a polythene tube in the abdominal aorta; the intrarenal pressure of both kidneys was obtained via needles in the cortices; all the pressures were measured with capacitance manometers (M)

In three dogs the renal perfusion pressure to both kidneys was lowered suddenly to about 20 mm Hg for five minutes by inflating a small soft-rubber balloon inserted into the descending thoracic aorta via the right carotid artery This manœuvre which was repeated several times in each dog was accompanied by a slight transient rise in pressure proximal to the balloon In these experiments the arterial pressure in the abdominal aorta was measured with a capacitance manometer via a polythene catheter inserted through the right femoral artery (fig 1)

In three dogs the necrosed kidney was decapsulated with a curved blunt probe and rat toothed dissecting forceps care being taken to handle the kidney as little as possible After decapsulation thirty minutes was allowed to elapse before the intrarenal pressure measurements were repeated

At the end of the experiments the dogs were killed with an overdose of pentobarbitone and both kidneys were removed weighed and examined histologically

## Results

*Pathology*

The accompanying table gives the length of time the left renal artery was occluded the weight of both kidneys, and a rough indication of the extent of the structural damage found in the left kidneys

EFFECTS OF OCCLUSION OF LEFT RENAL ARTERY

| Dog no | Duration of occlusion (hr ) | Weight of kidneys (g ) |  | Histology of left kidneys |  |
|---|---|---|---|---|---|
|  |  | Control | Necrotic | Cortex | Medulla |
| 1 | 4 5 | 42 | 51 | + + + | + + + |
| 2 | 4 5 | 40 | 54 | + + | + + |
| 3 | 4 0 | 35 | 42 | + + | – |
| 4 | 3 5 | 33 | 34 | + + | – |
| 5 | 3 0 | 40 | 33 | + + | – |
| 6 | 3 5 | 20 | 24 | + | – |
| 7 | 3 5 | 35 | 40 | + + | + + |
| 8 | 3 5 | 26 | 30 | + + | – |

+ + + complete necrosis.
+ + extensive necrosis interspersed with patches of normal structure
+ necrotic and normal areas about equal.
– no evidence of damage to cells

The left kidneys were firmer larger and heavier than the control (right) kidneys , the mean weight of the left kidneys was 38 5 g and that of the right kidneys 33 5 g The histological appearances of the tubules in the cortices of the left kidneys varied from necrosis of the whole cortex to extensive necrosis interposed with local patches of relatively normal tubules. The least affected areas in the cortices of all the necrosed kidneys were in the region of the juxtamedullary glomeruli and in three dogs there were thin scattered areas of normal cortex lying immediately beneath the capsule

The pathological changes in the medullæ of the left kidneys were as follows in one dog complete necrosis in two others scattered areas of necrosis in the remainder the appearances were normal except for colloid casts found in most of the medullary luminæ of all the left kidneys

*Cortical Intrarenal Pressures*

Figs 2 and 3 illustrate the result of all needle insertions

Each point in fig 2 represents the intrarenal pressure obtained from each insertion of the needle into sites where the pressure was relatively stable In some sites, however, particularly in the necrosed kidney the intra renal pressure fluctuated considerably (fig 4) the extent and frequency of this phenomenon are shown in fig 3 where each vertical line represents the highest and the lowest pressures obtained at separate insertions of the needle All insertions of the needle where the pressure fluctuated by more than 10 mm Hg are represented in those control kidneys (dogs 1 4 and 8) where fluctuations of this order were not observed the next largest fluctuation has been shown

The intrarenal pressures obtained from areas relatively free from fluctuations showed a fairly wide scatter on the control side with an even greater scatter on the necrosed

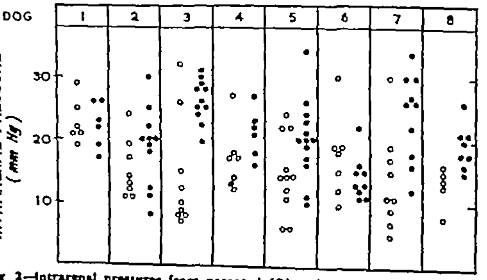


Fig 2—Intrarenal pressures from necrosed (○) and control (●) kidneys of eight dogs obtained by inserting needles into sites where pressures were relatively stable.

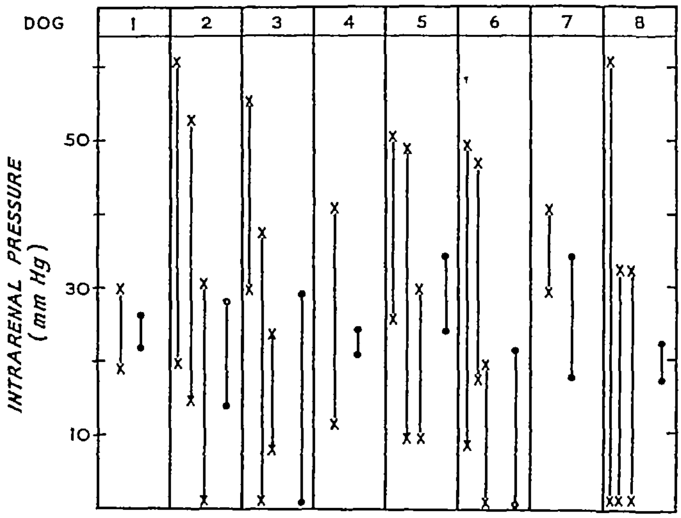


Fig 3—Intrarenal pressures from necrosed (×) and control (●) kidneys of eight dogs, obtained by inserting needles into sites where pressure was fluctuating Each vertical line represents highest and lowest pressures obtained from separate insertions of needle into areas where pressure fluctuated by more than 10 mm Hg In dogs 1, 4, and 8, in which no such fluctuations took place in control kidney, next largest fluctuations are shown

side (fig 2) The mean intrarenal pressure of the control kidneys was 22 mm Hg, and that of the necrosed kidneys 16 mm Hg

Fig 3 shows that pronounced fluctuations in pressure were more common and more extensive in the necrosed than in the control kidneys In the necrosed kidneys fluctuations might consist of irregular swings ranging from 0 to 50 mm Hg in ten to thirty seconds, at other times an initial pressure well above the mean would immediately begin to drift gradually and steadily to levels near 0 mm Hg In the control kidneys irregular fluctuations were seen on occasions but pressures did not swing far from the mean, a gradual drift down to very low pressures was also seen occasionally, but the point from which the drift would start was never far from the mean

### *Effect of Sudden Severe Reduction of Renal Arterial Pressure on Cortical Intrarenal Pressure*

Fig 5 shows the intrarenal pressure before, and five minutes after, the renal arterial pressure had been lowered to about 20 mm Hg The intrarenal pressure was substantially reduced in both the necrosed and the control kidneys, and after five minutes' hypotension the intrarenal pressure in the necrosed kidneys was slightly lower than in the control kidneys, the mean pressure being 7 mm Hg and 4 mm Hg respectively

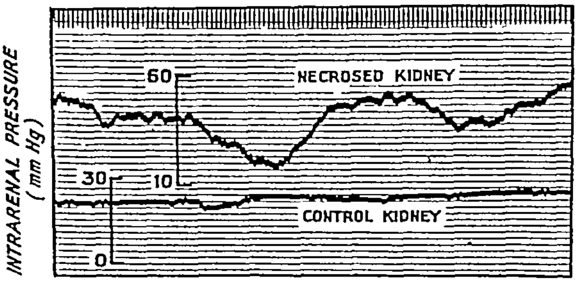


Fig 4—Continuous recording (in dog 6) of intrarenal pressure in necrosed (upper tracing) and contralateral control kidney (lower tracing) showing wide fluctuations in necrosed kidney

Fig 6 is a record of one of these experiments in dog 3 The needle in the necrotic kidney was in an area where there were occasional severe fluctuations in pressure, the renal arterial pressure being lowered while the intrarenal pressure was relatively high (40 mm Hg) and stable The reduction in renal arterial pressure was accompanied by a rapid reduction of the intrarenal pressure both in the necrosed and in the control kidneys, the rate of decrease being about the same in both Five minutes later, however, when the arterial pressure was allowed t return to normal, the rise of the intrarena pressure in the necrosed kidney was more rapid than in the control kidney, this disparity recorded in eight of the eleven occasions on which the experiment was performed

Fluctuations in the intrarenal pressure wer never obtained when the renal arterial pressur was low

### *Effect of Decapsulation on Intrarenal Pressure o Necrosed Kidney*

Fig 7 shows the intrarenal pressure of th necrosed kidney before, and thirty minutes afte the capsule had been removed, there was n appreciable change of pressure

## Discussion

The procedure used to produce renal damage i these experiments was similar to that which, has been shown, will produce histological chang identical with those found in human tubular necro (Oliver et al 1951), except that in man the lesions a usually less widely distributed It has also been show both in man (Bull et al 1950) and in animals (Phill et al 1945), that such lesions are associated with sustain severe renal ischæmia

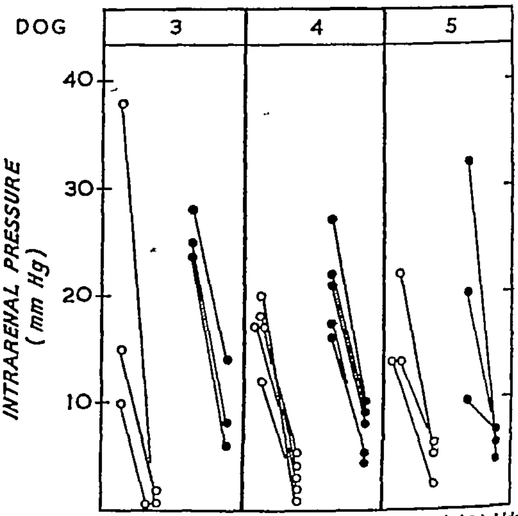
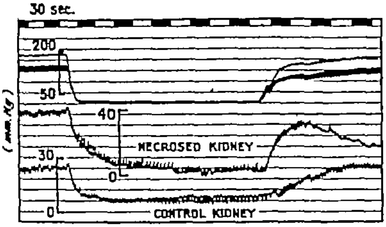


Fig 5—Intrarenal pressures of necrosed (O) and control (●) kid immediately before, and five minutes after, the abdominal aor pressure had been suddenly reduced to about 20 mm Hg, show the fall in intrarenal pressure which followed The experim was made three times in dogs 3 and 5, and five times in dog 4.

There is no histological evidence that intravascul thrombosis of renal vessels occurs either in tubular necros in man or in experimental tubular necrosis produce by transient occlusion of the renal artery in dogs Th sustained renal ischæmia accompanying tubular necros must therefore be due either to vasoconstriction or compression of the vascular tree It is clearly not due compression of the renal arterioles, for no pressu obtained inside the necrotic kidney was of sufficie magnitude to do this, but compression of the peritubul venous capillaries and interlobular veins is a possibility either by an increase in the interstitial fluid pressure o by an increase in the size of the tubules If this were th primary cause of the renal ischæmia, however, th inevitable consequence of such compression would be



-Continuous recording (in dog 3) of abdominal aortic pressure rmost tracing) intrarenal pressure of necrosed kidney (middle ng) and intrarenal pressure of control kidney (lowermost ng) before, during and after inflating a rubber balloon in the nding thoracic aorta for five minutes. As arterial pressure fell renal pressure of necrosed kidney decreased to the same low level ut of control kidney The small sharp fluctuations in pressure th intrarenal-pressure tracings are due to respiratory movements.

derable rise in the peritubular venous capillary ure The evidence presented here and discussed y gives no indication of such a rise so it is concluded the ischæmia is due to arteriolar constriction

e pressure measured by plunging a needle into the tance of the kidney is not only that of the interstitial r An inspection of the needle in the cortex of the ey makes it evident that the pressure obtained will be ved not merely from the pressure existing between the hrons and the peritubular capillaries (the interstitial re) but also from that existing within these structures s is the reason that the less precise term the intrarenal sure is used Swann (1951) has shown that the intra al pressure is almost certainly obtained from the lumina the torn peritubular capillaries and interlobular veins he found that the pressures measured with a needle the cortex of the kidney and from a catheter introd ed into an arcuate vein are identical (20–25 mm g). The renal venous pressure is about 10 mm Hg d the change to 20 mm. Hg appears sharply at the ction of the arcuate and the interlobar veins, where man et al. (1953) have demonstrated valve and hincter-like organs by which they suggest the peri bular venous pressure is controlled. Rapid fluctuations the intrarenal pressure also strongly suggest that the dle is measuring an intravascular pressure (Miles and Wardener 1954) If blood is to flow, the extravascular or interstitial, pressure must be lower than this intra vascular pressure but the gradient between the two is problematical the flatness of the peritubular capillaries and the thinness of their walls make it unlikely that it is very great

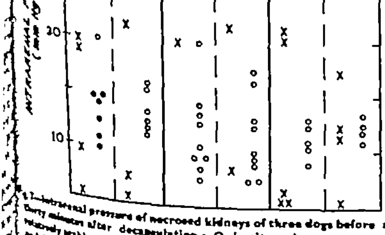
The results given here show that the intrarenal pressure in the cortex and medulla of an experimentally necrosed dog's kidney is similar to or less than, that of the contra lateral control kidney except that in the necrosed kidney severe fluctuations in pressure are often found (up to 60 mm Hg) They also show that when the descending thoracic aorta is occluded, the intrarenal pressure in both the necrosed and the control kidneys decreases to very low levels and that fluctuations no longer occur the intrarenal pressure of the necrosed kidney being then a little lower than that of the control kidney

It may therefore be concluded that the pressure measured in both the necrotic and the normal kidneys is derived from the heart The relatively low pressure obtained however and the absence of pulsations greater than 5 mm Hg indicate that in both kidneys the pressure that is measured is not obtained from the arterial side of the renal circulation The pressures in the necrotic and control kidneys are similar so, if it is accepted that in both kidneys the lumina of the needles are in con tinuity with torn peritubular venous capillaries and that the intrarenal pressure in the control kidney is a measure of the pressure within these capillaries it follows *that the peritubular venous capillary pressure in the* necrosed kidney whatever its value is not raised above normal It then follows that the sustained renal ischæmia that these necrotic kidneys must undoubtedly have had was due to arteriolar constriction and not to compression of the peritubular capillaries. The finding that during hypotension the intrarenal pressure in the necrotic kidney is slightly lower than in the control kidney is additional evidence that the renal interstitial pressure is not raised

The exact mechanism responsible for fluctuations in intrarenal pressure is uncertain but as they can occur independently of changes in systemic pressure and cease with occlusion of the aorta, they appear to be related to local vascular phenomena initiated by changes in vascular tone Previous observations with adrenaline and bleeding have certainly shown that changes in the intrarenal pressure can be induced by changing vascular tone (Miles and de Wardener 1954) The increased fluctuations in the intrarenal pressure of the necrosed kidney therefore probably reflect an increase in the variability of vascular tone an observation which supports the conclusion that *renal ischæmia is due to severe vasoconstriction for* instability is a characteristic of high vascular tone (Guyton and Harris 1951) This instability is particularly conspicuous in the kidney and can often be observed when a highly vasoconstricted kidney is perfused with a constant-output pump (unpublished observations)

The stimulus for the sustained vasoconstriction of tubular necrosis is a matter of speculation it may be due to metabolites released from damaged tubules acting on the vessels directly or on the intrarenal nervous ganglia , or perhaps the primary renal ischæmia produces anoxic changes in these ganglia which perpetuate the vaso constriction

Though there is no evidence that in the necrosed kidney the pressure of the renal interstitial fluid is raised, the histological appearances suggest that its volume is increased Such an accumulation would account for the increase in weight and volume of the kidney and probably though less obviously, for its increased firmness An object is firm to the touch in so far as it resists changes in shape The surface of the normal kidney is easily depressed owing to the fact that the fluid inside the kidney lies within relatively distensible tubes. When the surface is pressed at one point, much



2—Intrarenal pressure of necrosed kidneys of three dogs before and thirty minutes after decapsulation : O in sites where pressure was relatively stable ; X in sites where pressure was fluctuating highest and lowest pressures obtained at each such site being shown.

of the fluid lying beneath this point can be rapidly displaced elsewhere In the necrotic kidney, however, the accumulation of interstitial fluid lies outside these tubes, unable to move quickly when pressed on, with the result that the kidney feels firm on palpation

The ineffectiveness of decapsulation on the intrarenal pressure of the necrosed kidney is in keeping with recent work showing that, in a normal kidney, even large induced changes in intrarenal pressure are not modified by the presence or absence of the capsule (Miles and de Wardener 1954)

## Summary

The intrarenal pressure in dogs was measured with a capacitance manometer via a needle introduced into the substance of the kidney

The left kidney was made ischæmic for three to four and a half hours, two to four days before the intrarenal pressure was measured

The intrarenal pressure of the left (necrosed) kidney was measured simultaneously with that of the right (control) kidney, and the pressure in both was found to be similar, except that in some areas of the necrosed kidney there were large fluctuations in pressure

When the descending thoracic aorta was suddenly occluded, the intrarenal pressure of both kidneys fell to very low levels, and fluctuations ceased

Decapsulation of the necrosed kidney had no effect on the intrarenal pressure

It is concluded that the sustained renal ischæmia of tubular necrosis is due to vasoconstriction rather than to a raised renal interstitial pressure

I wish to thank Dr H. Spencer for help with the histology, and Messrs M G Ventom and R F Schofield for technical assistance

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# STAPHYLOCOCCAL INFECTION IN THE NEWBORN

## TREATED WITH ERYTHROMYCIN

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STAPHYLOCOCCAL infection develops in about 10–15% of infants born in large maternity units (Nelson 1952, Barber et al 1953, Edmunds et al 1955) In such units lococci isolated both from cases of clinical infection and from nasal carriers commonly show resistance, in some degree, to the antibiotics in common use For example, resistance to penicillin can now be demonstrated in 50–80% of hospital strains of *Staphylococcus pyogenes*, and resistance to the tetracyclines is increasing steadily (Kirby and Ahern 1953)

Satisfaction at the introduction of erythromycin, another antibiotic effective against the staphylococcus, has been tempered by the fear that resistance might develop rapidly if it were extensively used Resistance in staphylococci has been readily induced in vitro (Hobson 1954), and resistant staphylococci have appeared after the regular use of erythromycin to control infection in burns (Lowbury and Cason 1954) and after prolonged treatment with erythromycin in subacute bacterial endocarditis (Haight and Finland 1952) It is in cases of this type that resistance might be expected, but experience of erythromycin in the treatment of staphylococcal infection has been insufficient for the proper assessment of the risk of resistance developing in ordinary hospital practice (Herrell et al 1953, Kirby et al 1953) Fortunately there does not seem to be cross resistance between erythromycin and other antibiotics in common use

## Present Investigation

The present investigation was designed to test the efficacy of erythromycin in neonatal staphylococcal infection and particularly to determine whether resistance would appear quickly under controlled conditions

The trial took place in the maternity units of two hospitals. In Hospital E all clinical infections were treated with oral erythromycin (' Ilotycin ' suspension) 20 mg per lb of body-weight daily in divided doses given six hourly In Hospital W clinical infections were treated with the same dosage of erythromycin at the same intervals, but in addition a daily injection of streptomycin (0 125 g) was given It was hoped by this means to determine whether combined therapy would reduce the risk of resistant strains emerging Streptomycin was chosen because in these units 80% of strains of *Staph pyogenes* were sensitive to it (Forfar et al 1953)

As a preliminary to the trial a survey of antibiotic sensitivity was made in Hospital W by examining 46 consecutive swabs from the cord stumps of infants at the time of separation

In Hospital W during the trial, and in both hospitals at the end of the trial, nasal swabs were taken from the staff and examined for *Staph pyogenes* Throughout the trial swabs were taken from clinical infections wherever practicable

The trial continued for nine months During this time 140 infants in Hospital E were recognised as having a staphylococcal infection and received erythromycin therapy In Hospital W 112 infants became infected, but only 80 of these were treated, receiving erythromycin and streptomycin The smaller number treated in this hospital is explained by the fact that the pressure on accommodation enforced a shorter stay and made it impossible to retain babies for the treatment of trivial sepsis developing near the time for the mother's discharge, when suitable treatment could be given at home About 1 of every 7 infants born in Hospital E was treated with erythromycin, and about 1 of every 10 infants born in Hospital W received erythromycin and streptomycin

During the period of the trial no other systemic antibiotic was used in either unit Local preparations of antibiotics were banned, the only exception being the treatment of an occasional case of conjunctivitis with chloramphenicol drops after systemic therapy had failed.

Every effort was made to record all clinical infections, however trivial Edmunds et al (1955) show that early recognition and early treatment of minor staphylococcal infection of the newborn play an important part in preventing serious sepsis During the nine months of this

BLE I—ANTIBIOTIC SENSITIVITY OF STRAINS OF *Staph pyogenes* ISOLATED FROM CASES AND NASAL CARRIERS

| Source | No of strains | Percentage of strains resistant to | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | P | S | C | CT | O | E | SU |
| rds (Hospital W) | 35 | 86 | 22 | 20 | 11 | 14 | Not tested | 20 |
| fections (Hospital W) | 65 | 85 | 22 | 17 | 0 | 0 | 0 | 20 |
| fections (Hospital E) | 87 | 75 | 21 | 8 | 11 | 11 | 0 | 30 |
| sal carriers (Hospital W) | 36 | 84 | 33 | 14 | 6 | 6 | 0 | 30 |
| sal carriers (Hospital E) | 26 | 80 | 8 | 4 | 8 | 8 | 0 | 38 |

chloramphenicol. CT chlortetracycline. E, erythromycin. xytetracycline. P penicillin S streptomycin. SU, sulphonamide

tal no serious staphylococcal infection occurred in ther unit.

## Clinical Results

The incidence of clinical infection was 14% in Hospital W nd 13% in Hospital E Of the 140 babies with clinical fection in Hospital E, 89 (64%) had conjunctivitis, 10 4%) had skin pustules, 13 (9%) had infection of the mbilical stump 9 (6%) had local cellulitis or paronychia nd 10 (7%) were not adequately documented. The 112 ses of clinical infection in Hospital W comprised 68 ses of conjunctivitis (61%) 27 of skin pustules (24%), 4 fections of the cord stump (4%) and 13 cases of llulitis or paronychia (11%)

Of the 140 cases treated in Hospital E swabs were not ken in 26—chiefly minor skin infections Of the 114 amined bacteriologically a coagulase-positive staphylococcus was grown in 84 (74%) a coagulase negative aphylococcus in 21 (18%) and some other organism in (3%). All the 80 cases treated in Hospital W were amined bacteriologically In 56 (70%) a coagulase sitive staphylococcus was isolated in 20 (25%) a agulase-negative staphylococcus and in 2 (2 5%) other ganisms. In 2 cases (2 5%) no growth was obtained

The average duration of treatment in Hospital E was 5 days, with a range of 2–8 days and in Hospital W 4 days with a range of 2–9 days In each case treatment was stopped when clinical cure was established

BLE II—BACTERIOPHAGE GROUP AND ANTIBIOTIC SENSITIVITY OF STRAINS OF *Staph pyogenes*

<table>
<tr><th rowspan="2">Source</th><th rowspan="2">No of strains</th><th rowspan="2">Phage group</th><th colspan="8">No of strains</th></tr>
<tr><th colspan="2">PS : SS and sensitive to other antibiotics</th><th colspan="2">PR : SS and sensitive to other antibiotics</th><th colspan="2">PR : SR and sensitive to other antibiotics</th><th colspan="2">PR SR CR and/or CTR OR</th></tr>
<tr><td>Cords (Hospital W)</td><td>35</td><td>Not examined</td><td colspan="2">5</td><td colspan="2">3*</td><td colspan="2">1</td><td colspan="2">7</td></tr>
<tr><td rowspan="4">Infections (Hospital W)</td><td rowspan="4">65</td><td>I</td><td>4</td><td rowspan="4">10</td><td>19</td><td rowspan="4">37</td><td>4</td><td rowspan="4">8</td><td>1</td><td rowspan="4">10</td></tr>
<tr><td>II</td><td>3</td><td></td><td></td><td></td></tr>
<tr><td>III</td><td>2</td><td>15</td><td>4</td><td>9</td></tr>
<tr><td>Not typable</td><td>1</td><td>3</td><td></td><td></td></tr>
<tr><td>Infections (Hospital E)</td><td>87</td><td>Not examined</td><td colspan="2">20</td><td colspan="2">40</td><td colspan="2">7</td><td colspan="2">9</td></tr>
<tr><td rowspan="4">Nasal carriers (Hospital W)</td><td rowspan="4">30</td><td>I</td><td>2</td><td rowspan="4">6</td><td>10</td><td rowspan="4">18</td><td>4</td><td rowspan="4">7</td><td>1</td><td rowspan="4">5</td></tr>
<tr><td>II</td><td></td><td>1</td><td>1</td><td></td></tr>
<tr><td>III</td><td>4</td><td>5</td><td>2</td><td>3</td></tr>
<tr><td>Not typable</td><td></td><td>2</td><td></td><td>1</td></tr>
<tr><td rowspan="4">Nasal carriers (Hospital E)</td><td rowspan="4">26</td><td>I</td><td>4</td><td rowspan="4">5</td><td></td><td rowspan="4">19</td><td></td><td rowspan="4">0</td><td></td><td rowspan="4">2</td></tr>
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<tr><td>Not typable</td><td></td><td>5</td><td></td><td>1</td></tr>
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CR chloramphenicol-resistant. CTR, chlortetracycline resistant
OR, oxytetracycline-resistant. PR, penicillin resistant
PS, penicillin-sensitive. SR, streptomycin resistant.
SS, streptomycin-sensitive

Satisfactory control of infection was achieved rapidly in most cases In Hospital E, 6 cases did not respond these were all eye infections, of which 5 were associated with coagulase positive staphylococci and 1 with an atypical *Escherichia coli* Although local factors in the eye may delay response we have for this study listed these cases as failures. The failure rate for conjunctivitis was therefore 6 out of 89 cases (6 8%)

In Hospital W 4 cases did not respond to treatment with erythromycin and streptomycin; these again were all eye infections From 2 of them coagulase positive staphylococci were isolated, and from the other 2 no pathogens were obtained The failure rate for conjunctivitis in this hospital was therefore 4 out of 45 cases (8 9%) No comparable figures are available for systemic treatment with other antibiotics because it is our normal practice to use local antibiotic therapy predominantly for conjunctivitis

No failures occurred in either hospital in the response of superficial and deep skin infections No difference was recognised between the response to erythromycin alone and the response to erythromycin and streptomycin combined

TABLE III—BACTERIOPHAGE TYPE OF STRAINS OF *Staph pyogenes*

| Bacteriophage | | No of strains isolated from | | |
|---|---|---|---|---|
| Group | Type | Hospital W | | Hospital E carriers |
| | | Patients | Carriers | |
| I | 52/5*A | *4 | 15 | 2 |
| | Others | 4 | 2 | 0 |
| II | 3A/3B/3C/51 | 3 | 2 | 3 |
| III | 76/77 | 9 | 2 | 0 |
| | 6/7/47/76/77 | 8 | 8 | 0 |
| | 53/75/77 | 6 | 2 | 1 |
| | 6/7/47/53/54/75/77 | 0 | 0 | 9 |
| | 7/53/75 | 0 | 0 | 5 |
| | Others | 7 | 2 | 0 |
| NT | Not typable | 4 | 3 | 6 |

Newborn infants take erythromycin readily vomiting was noted very seldom and was never troublesome To 1 infant four times the above dosage was given inadvertently for seven days and caused only slight vomiting No diarrhœa was noted in treated infants In no case did clinical thrush develop as a complication of treatment during the stay in hospital.

## Bacteriology

Swabs of pus and exudate from the cases under examination, and nasal swabs from the attendants, were inoculated on to blood agar plates with the minimum of delay Coagulase positive *Staph pyogenes* were subcultured and tested for antibiotic sensitivity (Gould and Bowie 1952) and bacteriophage type (Williams and Rippon 1952) The results are shown in tables I–III

All strains of *Staph pyogenes* resistant to penicillin 0 15 unit per ml. were classified as penicillin resistant and it was found that they all produced penicillinase Strains were also classified as resistant to streptomycin chloramphenicol chlortetracycline (aureomycin) and oxytetracycline (terramycin) when their minimum inhibitory concentrations exceeded 5 10 10 and 10 µg per ml respectively

All strains of *Staph pyogenes* were inhibited by erythromycin 0 5 µg per ml Since the systemic level usually attained during therapy is about 5 µg per ml. these strains can be regarded as highly sensitive

No strain sensitive to penicillin was resistant to any other antibiotic tested and no strain resistant to penicillin but sensitive to streptomycin was resistant to any of the other antibiotics (table II) The strains resistant to penicillin have been divided into three groups (1) those which were sensitive to streptomycin and the other antibiotics , (2) those which were resistant to streptomycin but sensitive to the other antibiotics , and (3) those which were resistant to streptomycin and to one or more of the other antibiotics (table ii)

*Umbilical cord Swabs (Hospital W)*

*Staph pyogenes* was isolated from 35 umbilical swabs (76%) The antibiotic resistance of these strains is shown in tables i and ii 5 strains (14%) were sensitive to all the antibiotics tested , 30 (86%) were resistant to penicillin, and 8 of these were resistant to streptomycin The bacteriophage type of these strains was not determined

*Clinical Infections (Hospital W)*

*Staph pyogenes* was isolated from 65 cases 10 of these strains (15%) were sensitive to all the antibiotics tested and had bacteriophage types quite different from the remainder of the strains in this particular group 55 (85%) were penicillin-resistant, and 18 of these were also resistant to streptomycin Most of the penicillin-resistant strains belonged to one or other of four well defined phage types 52/52A, 76/77, 6/7/47/76/77, and 53/73/77 (table iii)

*Clinical Infections (Hospital E)*

*Staph pyogenes* was isolated from 84 cases 19 of these strains (23%) were sensitive to all the antibiotics tested , 65 (77%) were penicillin-resistant, and 18 of these were also resistant to streptomycin The bacteriophage type of these strains was not determined

*Attendant Staff in Hospital W and Hospital E*

The staff of the maternity unit in Hospital W was examined on two occasions during the investigation for nasal carriage of *Staph pyogenes* 32 (38%) were found to be carriers 6 of the 36 strains isolated (16%) were sensitive to all the antibiotics tested , 30 (84%) were penicillin resistant, and 12 of these were also streptomycin resistant The antibiotic sensitivities and bacteriophage types corresponded to those of the strains isolated from the patients with clinical infection The phage-types were quite different from those of the strains isolated from the staff carriers in Hospital E

The maternity-unit staff of Hospital E was similarly examined on one occasion, and 26 (70%) were found to be nasal carriers 5 (20%) of the strains isolated were sensitive to all the antibiotics tested, 21 (80%) were penicillin resistant , and the majority belonged to two well defined phage-types 6/7/47/53/54/76/77 and 7/53/73 (table iii)

Among the various groups of swabs, umbilical, nasal, and clinical infection, chloramphenicol resistance ranged from 4% to 20%, chlortetracycline resistance from 6% to 11%, and oxytetracycline resistance from 6% to 14%

*Effect of Erythromycin on Intestinal Flora*

In view of the possible disturbance of the intestinal flora, specimens of fæces from 30 cases in Hospital W were examined bacteriologically *Esch coli* was isolated from all the specimens, and all of the strains were resistant to erythromycin 50 µg per ml In no case was *Staph pyogenes* isolated

## Discussion

The limitations of this study must be clearly stated Erythromycin was used for only nine months and only in two maternity units The results may therefore not be generally applicable to more continued use in other circumstances None of the nurses was treated with erythromycin during the period of the study No local therapy was permitted , hence the chance that nurses might come into contact with the antibiotic was reduced to a minimum Many infants were treated, but only for relatively short periods, the longest being nine days, and the question of drug resistance developing during long-[illegible]ed treatment of the individual case did not arise

Before the trial no erythromycin had been used in these hospitals , penicillin had not been used in the nurseries, for routine treatment, for over two years , streptomycin had been used sparingly during a brief outbreak of gastro enteritis , chlortetracycline had been used regularly for a time but for the previous year had been replaced by oxytetracycline All of these antibiotics had been given systemically, and chlortetracycline had been given locally into the eye Chloramphenicol had been used regularly for the local treatment of neonatal ophthalmia, having taken the place of sulphacetamide solution for this purpose It is against this background that the results of the sensitivity tests must be assessed It should also be noted that both maternity units are parts of general hospitals, and that there is limited exchange of medical and domestic staff between them and other parts of the hospital

Erythromycin has proved useful in the treatment of staphylococcal infection and, where systemic therapy is indicated, appears to be as effective as other antibiotics It has at the moment a particular place in the treatment of staphylococcal infection in which other antibiotics have failed owing to drug resistance It is more successful in the management of skin sepsis than in the control of conjunctivitis, where it failed in about 8% of cases.

In most cases of conjunctivitis, which is the commonest type of staphylococcal infection of the newborn, systemic therapy is not indicated Local therapy probably has a lower failure rate, acts more quickly, and can be discontinued sooner For this we use chloramphenicol, which has the advantage that complete resistance of the staphylococcus to it seldom develops (Finland 1953) and cross resistance between it and other antibiotics is seldom observed (Fusillo et al 1953)

On the basis of in-vitro tests a high sensitivity rate of the staphylococcus to erythromycin has been shown In Edinburgh, before this investigation, we had not observed a naturally occurring erythromycin-resistant strain of *Staph pyogenes,* and during the nine months of this trial no erythromycin-resistant strains emerged Important factors contributing to this were (we believe) restricted use, adequate dosage, and careful technique in handling the antibiotic, whereby the likelihood of bacterial resistance developing quickly was reduced

Our experience has been in striking contradistinction to that of Lepper et al (1953), who found that, within a month of the adoption of erythromycin for general use in a hospital, strains of staphylococci resistant to it began to appear in the nose and throat of the staff, and that after five months the carrier-rate of highly resistant strains had reached 75% Encouraging as our results with erythromycin appear, and without detracting from the value of this new chemotherapeutic agent in the treatment of staphylococcal infection, one must appreciate the fact that all the strains isolated in this series were distributed between only a few phage types This means that the number of strains dealt with was in reality very limited Had erythromycin resistance developed in *one* of our phage-types, it would have appeared that all cases infected with this particular type had developed resistance, and this might have produced a high resistance rate At the same time some of the phage-types persisted throughout the trial, and these showed no evidence of developing erythromycin resistance

Resistance to any antibiotic other than penicillin was always accompanied by penicillin resistance Others have reported similar findings Finland and Haight (1953), for instance, note that it is exceptional to find a strain of *Staph pyogenes* resistant to chlortetracycline and oxytetracycline that is not also resistant to penicillin Apparently there is some relationship between penicillinase production and resistance to other antibiotics , and in hospitals, where penicillinase-producers are so common, this relationship is likely to be important The servoir of staphylococci among carriers in the population outside hospital still appears to consist largely of organisms sensitive to penicillin and if continuous selection by exposure to antibiotics could be avoided these might be expected to take the place of hospital strains.

In Hospital W, three years ago a series of swabs exactly similar to that taken in the present investigation—from the umbilicus and from clinical infections of the infant and from the nares of the staff—was examined (Forfar et al. 1953) It is of some interest to compare the antibiotic sensitivity of staphylococci over this three year period. If as the level of significance we accept two and a half times the standard error of the percentages tested, and if we compare staphylococci isolated from corresponding sites, we find that there has been no significant increase or decrease in resistance to penicillin, chloramphenicol, or chlortetracycline As regards the staphylococci carried by the staff however there has been a significant increase in streptomycin resistance In similarly comparing corresponding groups of swabs taken during the present investigation in Hospital W and in Hospital E we find that the only significant difference is between the staffs—the staphylococci carried by the staff in Hospital W again showing a significant increase in streptomycin resistance This higher incidence of resistance to streptomycin in Hospital W may be related to the greatly increased handling of that antibiotic by the nurses of the hospital during the trial owing to its routine use there

There is ample evidence of cross-infection in the units investigated, by either direct or indirect contact with carriers or cases. The number of penicillin resistant strains among both carriers and patients is striking; and, again, the most common sensitivity pattern (penicillin resistant: streptomycin-sensitive) is very evident in both. The evidence for cross infection is strengthened by the results of phage-typing not only do all the strains isolated fall into four distinct types but also particular phage patterns are common to both patients and carriers It therefore appears that the cases were infected inside hospital from staphylococcal carriers in contact with patients or from other patients.

In a few cases infection was by penicillin sensitive strains with a phage pattern similar to that of strains encountered outside hospital. Possibly the infection was maternal in origin but as some members of the staff also carried non hospital strains it could equally well have come from the staff

The natural resistance of all *Esch coli* isolated from faeces seems to show that the normal intestinal flora is not upset by erythromycin given for a short time (five days) in the dosage used

## Summary

In one maternity unit 140 cases of neonatal staphylococcal infection were treated with erythromycin In another unit 80 cases were treated with erythromycin and streptomycin

The average duration of treatment was about *four days* with a range of two to nine days There were *no failures* in the treatment of deep and superficial skin sepsis but a few cases of conjunctivitis did not respond Erythromycin with streptomycin proved no more effective than erythromycin alone

Phage typing showed that a limited number of strains were responsible for the cases of clinical infection

No strain of *Staph pyogenes* developed resistance to erythromycin during the trial. The extent of resistance to the other antibiotics and to sulphonamide is shown

Strains of the same antibiotic resistance pattern and phage type were isolated from the babies and from the staff showing that there was *free interchange* of staphylococci between staff and infants and between one infant and another and that cross infection was common

The increased use of streptomycin in one unit during the trial appeared to increase the proportion of streptomycin resistant organisms among staphylococci isolated from staff nasal carriers in that unit

Erythromycin did not interfere with the normal growth of *Esch coli* in the gut, and no case of fungus or staphylococcal infection of the alimentary tract was found

We wish to thank Prof T J Mackie for his interest and advice; Miss McIntyre Miss Cruickshank, Sister Moore and Sister Stephen of the two maternity units concerned for their coöperation; and Miss Margaret C Kelly B.SC Mr D J Annat F.I.M.L.T., and other members of the bacteriological departments for assistance Messrs Eli Lilly supplied the erythromycin

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# CŒLIAC DISEASE

## RESULTS OF LATE TREATMENT WITH GLUTEN FREE WHEAT DIET

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THE introduction of diets free from wheat gluten and rye gluten (Dicke 1950 Weijers and van de Kamer 1950) has not only simplified the treatment of cœliac disease but has also ensured that children with this disease grow at an optimal rate (Anderson et al 1952 Sheldon and Lawson 1952)

The reintroduction of wheat gluten into the diet leads to a gradual return of symptoms and a slowing down of the rate of growth (Dicke 1950, Anderson et al 1952) Merely slackening strict dietary control reduces the rate of growth even if other symptoms are absent (Sheldon and Lawson 1952 Gerrard et al 1955)

In a previous study (Gerrard et al 1955) we reinvestigated 32 children and adolescents who had been diagnosed as having cœliac disease in early childhood and had not been treated with gluten free wheat None of them was completely free from symptoms, but the symptoms were usually milder than initially Steatorrhœa stunted growth and anæmia were the commonest residual clinical findings

We report here the response of these older children to late treatment with a diet free from wheat gluten

### Patients and Methods of Investigation

Since management of the diet was to be the responsibility of the parents their full coöperation was necessary When the results of the above mentioned investigations became known the parents were given our find told that dietary treatment on modern lines c cate persisting symptoms and would probably ensure a more normal rate of growth and development They were warned that the diet was not easy to prepare, for it entailed the exclusion of many palatable foods and necessitated the baking of bread at home with specially prepared wheat starch They were also warned to expect not a dramatic change in their child's condition but a gradual improvement during three months, for this reason they were asked not to decide on the efficacy of the diet until it had been tried for at least three months

The parents of 22 patients decided to try the effect of the diet 4 of the patients remained on the diet for less than four months and have therefore been considered separately as defaulters The remaining 18, aged from 4 years to 16, included the most severe cases, they were losing an average of 8 3 g of fat daily in their stools, in contrast with a daily average loss of 7 0 g for the whole series of 32 children

Two main criteria were used for assessing the results of the diet growth estimated by measurement of height and weight, and the fat content of the fæces These investigations were made before treatment with gluten-free wheat and after at least four months on the diet, the length of treatment at the time of reassessment ranging from four to twenty-five months

*Growth*

Heights and weights were compared with the normal standards of Engelbach (1932) adapted by Wilkins (1950), for each child the percentage of the average weight and height for age was calculated

*Output of Fat in Fæces*

It was impossible to study fat balance in most of the children, because they were outpatients and their intake of dietary fat could not be accurately calculated For estimation of fat in the fæces complete five day collections of stools were obtained from all 18 children before treatment with the diet, and again from 16 of these at the time of reassessment The fat content of the fæces was estimated by a modification of the method described by van de Kamer et al (1949) Controls were obtained by investigating a five-day fæcal output of fat in each of 20 children in hospital convalescent from parenteral disorders and receiving the ordinary ward diet The average daily output of fat by each child was calculated from the five day figures

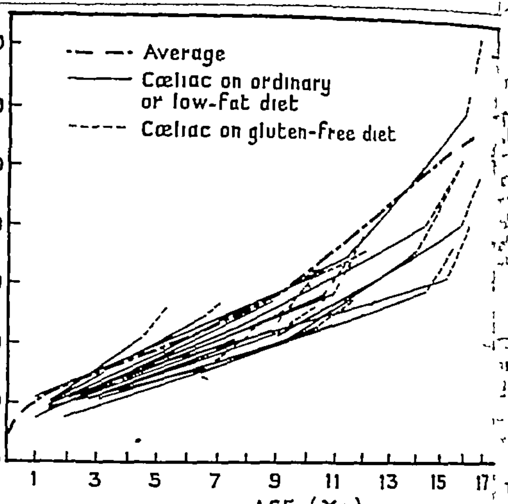
## Results

*Growth in Weight and Height*

When these children were initially reviewed, there was no reason to suspect that any was receiving an inadequate diet in the accepted meaning of the term, nor was anorexia a common persisting symptom Nevertheless on the new régime all 18 children began to gain weight and to grow in height more rapidly than before The accompanying table shows that, after a mean period of fourteen months on the diet, the mean percentage weight had increased from 82 7 to 92 8%, and the mean percentage height from 90 5 to 92 7% These differences are significant $P<0\ 001$ for both weight and height To make up so much of their earlier deficit so quickly they had, on average, gained in weight at two and a half times, and in height at twice, their previous rate The sudden alteration in the weight-gradient of each child after being put on the diet is shown in the accompanying figure The steep rise in the rate of growth will obviously flatten out as weights and heights approach normal

*Output of Fat in Fæces*

The table shows that before treatment the daily output of fat by the children ranged from 4 1 to 14 g (mean 8 3 g) At the time of reassessment on the diet the corresponding figures were 1 2–4 8 g (mean 3 4 g) These values were similar to those found in the 20 "normal" children 1 4–4 6 g (mean 2 7 g) The decrease in the fat content of the stools on gluten free [illegible] again statistically significant ($P<0\ 001$)



Increase of weight on different diets

*Other Factors*

The increased rate of growth and the diminution the fat-content of the stools are factors which could easily measured, but other less tangible improvemen were noted both by us and by our patients

A girl, aged 16, noticed that her finger nails required cutti every five or six days instead of once a fortnight as previous and that her hair also needed cutting much more frequent Others, on direct questioning, noted more rapid growth nails and hair In addition one girl, aged 7 years, who initi had dry and rather scanty hair, developed a thick glo growth while on the new diet

Two patients were troubled with furunculosis, possibly d either to better and more rapid assimilation of carbohydra or to the onset of puberty

Two girls, both aged 16, started to menstruate six wee and twelve months after being put on the diet In one these girls, who was still in hospital on a daily fat-balan menstruation was associated with an immediate but tempor diarrhœa and steatorrhœa, this disturbance of intestu function recurred regularly with succeeding menstrual peri

The vitality and demeanour of all the patien improved, the more obvious the persisting sympto had been the more striking was this improvement

*Defaulters*

3 of the 4 patients who abandoned the diet before fo months' trial were aged more than 15, they found th

EFFECT OF GLUTEN FREE WHEAT ON GROWTH AND ON OUTP OF FAT IN FÆCES

| Case | Age |  | Period on gluten free wheat (mos) | Percentage weight for age |  | Percentage height for age |  | Average fæcal f (g per day) |  |
|---|---|---|---|---|---|---|---|---|---|
|  | A | B |  | A | B | A | B | A | B |
|  | Yr Mos | Yr Mos |  |  |  |  |  |  |  |
| 1 | 4 7 | 5 3 | 8 | 119 0 | 133 0 | 103 0 | 102 0 | 6 6 | [illegible] |
| 2 | 6 5 | 7 0 | 7 | 109 0 | 112 0 | 98 0 | 98 5 | 9 1 | N<br>da |
| 3 | 6 8 | 7 11 | 15 | 70 0 | 84 0 | 81 0 | 83 0 | 6 5 | 4 |
| 4 | 7 6 | 9 0 | 18 | 85 0 | 91 0 | 89 0 | 90 0 | 6 6 | 3 |
| 5 | 8 10 | 10 3 | 17 | 80 5 | 99 0 | 94 0 | 97 0 | 8 5 | 4 |
| 6 | 8 10 | 10 2 | 16 | 97 0 | 102 0 | 93 0 | 93 5 | 8 5 | 2 |
| 7 | 9 0 | 10 10 | 22 | 76 0 | 82 0 | 92 0 | 93 5 | 10 0 | 3 |
| 8 | 10 3 | 11 9 | 18 | 70 0 | 71 5 | 84 0 | 87 5 | 14·0 | 4 |
| 9 | 10 7 | 11 4 | 9 | 84 0 | 94 5 | 86 0 | 89 0 | 14·0 | 3 |
| 10 | 10 8 | 12 2 | 16 | 93 5 | 92 0 | 92 0 | 92 5 | 4 1 | 1 |
| 11 | 11 1 | 12 0 | 11 | 81 0 | 99 5 | 88 0 | 91 0 | 5·0 | 4 |
| 12 | 11 11 | 12 3 | 4 | 65 0 | 69 0 | 84 0 | 85 0 | 7 3 | 1 |
| 13 | 14 0 | 16 1 | 25 | 72 0 | 95 0 | 91 0 | 96 5 | 12 3 | 4 |
| 14 | 14 4 | 15 7 | 15 | 62 5 | 71 0 | 83 0 | 88·0 | 11 5 | 2 |
| 15 | 14 7 | 15 10 | 15 | 78 5 | 91 5 | 97 0 | 100 0 | 4 6 | No<br>da |
| 16 | 15 3 | 16 5 | 14 | 59 5 | 71 5 | 80 0 | 85 0 | 10 0 | 3 |
| 17 | 16 0 | 16 10 | 10 | 75 0 | 87 0 | 94 0 | 96 0 | 6 4 | 4 |
| 18 | 16 1 | 17 0 | 11 | 111 0 | 125 0 | 101 0 | 101·0 | 4 9 | 4 |
| Mean |  |  | 14 | 82 7 | 92 8 | 90 5 | 92 7 | 8 3 | 3 |

A before treatment with gluten free wheat.
B, at time of assessment on gluten free wheat

erfered with their social activities Nevertheless all d improved on the régime and their parents were ited with the response:

irl, aged 10 had initially Hb 7 3 g per 100 ml this sed to 13 7 g per 100 ml. five months after the start of nent by diet and with oral iron.

oy aged 16 who had been lacking in vitality gained in two months and developed so much energy that he d a local cycling-club

irl, aged 14 put on 7 lb and 1½ inches in height in three hs and became livelier

## Discussion

e present study has shown that children and escents who have had cœliac disease for many years respond well to a diet free from wheat gluten It is evident that this diet is effective not only in the re phase of cœliac disease which is usually seen in y childhood but also in the latent or quiescent phase h is more commonly found in later childhood. The eased rate of growth observed in the present study erlines the importance of keeping these children on diet at least until active growth and development e ceased In some cases it may even be necessary to ntain the diet into adult life in view of the findings Cooke et al. (1953), who obtained a history of cœliac ease in childhold from many adults with idiopathic atorrhœa.

he increased rate of growth on gluten free wheat may e been partially due to an increased caloric intake ciated with an improvement in appetite That this not the sole reason was apparent from the concomi reduction in the output of fat in the fæces which rated an improvement in absorption of fat Anderson al (1952) have shown that the reduction in fæcal n cœliac disease after the start of treatment with t free from wheat gluten is associated with a rise he chylomicrograph count an increase in the glucose rance test, and a diminution in dilatation of the small stine All these findings indicate that there is a return stro-intestinal function to a more normal state

uring the progress of the work previously reported rard et al 1955) and the present study 2 children e observed whose symptoms of cœliac disease dated n the neonatal period—i e before they had begun to t wheat-containing foods. Although these 2 children normal pancreatic function, associated with steator a, they did not respond to gluten free wheat In view he early onset and their lack of response to the diet emed probable that the ætiology in these 2 cases different They have therefore been excluded from resent study

## Summary

he effect of a diet free from wheat gluten was investi ed in 18 children and adolescents who had been osed as having cœliac disease three to fourteen previously and had not recovered on diets con ng wheat flour

uring periods of from four to twenty five months on diet there was a striking acceleration of growth in ht and in height accompanied by disappearance of orrhœa

t is concluded that a diet free from wheat gluten is ful in both the active and the latent phases of e disease

e wish to thank the consultant staff of the Children s tal, Birmingham, for permission to study their patients A. C Frazer for his interest and encouragement Dr I. French for helpful advice and criticism Dr J A. H house for statistical analysis; and Miss M Cutler for ical assistance Finally we gratefully acknowledge ial assistance from the United Birmingham Hospitals rch Fund, the Medical Research Council and Messrs & Gale

*References at foot of next column*

# SICKLE-CELL TRAIT IN SOUTH TURKEY

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At Mersin on the southern coast of Turkey 15 cases of sickle-cell anæmia were found in a distinct and separate community of eleven families (Aksoy 1955), the patients included four pairs of siblings It was therefore interesting to determine the incidence of sickle-cell trait in this community whose ancestors had been immigrants to Turkey from Syria and Egypt several centuries ago and so far as is known had no Negro blood but had intermarried among themselves becoming inbred

## Method

The Scriver Waugh technique (Wintrobe 1951) was used at least two blood slides being made for each person

## Results

The blood was examined of 376 persons comprising two groups medical outpatients of Mersin State Hospital and their healthy relations and some of the inhabitants of a small village Çatalkeli near Tarsus For controls we used 200 persons who did not belong to this community Of the 376 persons 50 had sickle-cell trait (table I)

TABLE I—INCIDENCE OF SICKLE CELL TRAIT

| Group | No tested | No with sickle cell trait |
|---|---|---|
| Mersin city and vicinity | 181 | 25 (*13 8%*) |
| Çatalkoli | 195 | 25 (*12 8%*) |
| Total | 376 | 50 (*13 3%*) |
| Controls | 200 | 0 |

The persons tested were predominantly adults, but the second group consisted mainly of school children their ages ranged from 9 months to 72 years The numbers of males and of females were about equal

TABLE II—PERCENTAGES OF SICKLE-CELLS IN FIFTY PERSONS WITH SICKLE CELL TRAIT

| Percentage of sickle-cells | No of persons |
|---|---|
| 20–30 | 2 |
| 30–40 | 9 |
| 40–50 | 13 |
| 50–60 | 6 |
| 60–70 | 8 |
| 70–80 | 12 |
| Total | 50 |

The sickling phenomenon was usually positive before twenty four hours but sometimes started in three or four hours We got no positive results after the sickling phenomenon had been negative for twenty four hours and therefore do not expect any change after this period of time This observation confirms that of Watson et al

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(1948) The percentages of sickle cells found in the 50 cases of sickle cell trait are shown in table II

### Discussion

The present investigation showed a fairly high incidence (13 3%) of sickle cell trait This result is important not only because the people are white but also because it is the highest incidence of sickle cell trait found outside Africa (Jelliffe et al 1954, Neel 1951, Singer 1951) except in some tribes of Southern India (Lehmann and Cutbush 1952a and b) Caminopetros (1952) reported the very high incidence of 49 1% in Athens, but this has been disputed by Lehmann (1952) and Choremis (1952)

A high incidence of sickle cell anæmia has also been reported from Greece (Choremis et al 1951) and Italy (Silvestroni and Bianco 1952), but never have so many cases of sickle cell anæmia been found in a white community as in that of Southern Turkey All other cases of sickle cell anæmia in the white race have been isolated ones (Cooley and Lee 1929, Rosenfeld and Pincus 1932, Clarke 1933, Haden and Evans 1937, Johnson and Townsend 1937, Cooke and Mack 1934, Weiner 1937, Greenwald and Burrett 1940, Mallory 1943, Ogden 1943, Guyton and Heinle 1950, Abbasy 1951)

The fairly high incidence of sickle cell trait in the Turkish community reported here is expected from Neel's genetic theory for sickle-cell anæmia and for sickle cell trait (Neel 1949, 1951, 1952)

How can we explain this fairly high incidence of sickle-cell trait in the white community? At present the two most widely held opinions are as follows

(1) There was an admixture of Negro blood during either the Roman or the Turkish empires, or else in the era of medieval Mohammedan expansion

(2) Sickle cell trait spread to East Africa by the immigration of tribes from India (Lehmann and Cutbush 1952a and b) Jelliffe et al (1954) suggest that sickle cell trait may have spread from India to other places also, including the Mediterranean countries

Both of these explanations may fit the incidence of sickle cell trait in Southern Turkey To determine which of them is the better in the present case a thorough investigation of blood-groups should be undertaken, as was done in Southern India by Lehmann and Cutbush (1952a and b)

### Summary

In 376 persons belonging to a distinct and separate community in Southern Turkey the incidence of sickle cell trait was 13 3%

The possible explanations of this high incidence of sickle-cell trait in a white community are discussed

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# ŒSOPHAGEAL REFLUX AND THE ACTION OF CARMINATIVES

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ŒSOPHAGEAL reflux is common, but its mechanism obscure In patients with symptoms of reflux it depen on the relative positions of the structures forming th cardia, for it takes place only during inspiration an more commonly in some postures than others (Cream 1955) Nevertheless the normal cardia is compete under these conditions, and even when hiatus herniati is present there may be no reflux Clearly there must some change at the cardia that renders it susceptible these positional factors

In an attempt to define this change a search w made for drugs that would produce reflux in health people O'Mullane (1954) has shown that local a general anæsthesia, ganglion-blocking agents, and mus relaxants are all without effect on the competence of t cardia Since the same changes in pressure take pla whether gas or fluid is refluxed from the stomach, t action of carminatives on the cardia was investigat The following observations are based on recordings intra œsophageal and intragastric pressures and direct observation of the action of carminatives on t gastric mucosa by gastroscopy

### Methods

The intra œsophageal and intragastric pressures w measured through fine 'Polythene' tubes by Hans capacitance manometers (Dornhorst et al 1954a) these experiments the recording apertures were 5 c apart, and the tubes were so placed that one lay in t stomach and two in the œsophagus In each experim control observations were made with the subject various postures to test the competence of the car before giving carminatives In all the subjects test the cardia was shown to be competent After the subj had drunk the carminatives, continuous recordings of pressures were made for fifteen minutes 10 healt people and 6 patients with some specific abnormal were examined

The gastroscopic observations were made on 6 pati undergoing routine investigations for symptoms dyspepsia The carminatives were introduced into stomach through a fine polythene tube attached to gastroscope These patients were premedicated w 'Omnopon' and hyoscine (for details of local anæsthe see below)

*Carminatives*—These drugs belong to the group volatile oils, and most of the commonly used preparati are alcoholic solutions The following preparations w investigated

(1) Tinct cardamom co *B P 1953*
(2) Tinct cardamom aromat *B.P C 1949*
(3) Aq anethi conc *B P 1948*
(4) An emulsion of oil of dill in water

These were used in the *B.P* dosage All were found have the same effect, excluding that of the alcol present in the tinctures

### Results

When carminatives are given to a healthy pers there follows a constant pattern of events Almost once a sensation of warmth is felt in the epigastrium a sometimes also in the substernal region After two five minutes this is followed by a sensation of distensi in the epigastrium and a desire to belch This is variou described as flatulence, wind, or feeling blown out the erect posture eructation takes place in almost eve ease within fifteen minutes of taking the drug After this time the sensation of dis tension disappears. Eructation is almost as ensitive an index of the action of carmina ives as are intra-œsophageal recordings and as used in a few cases to confirm the results

*ressure Observations*

The changes which take place in intra œsophageal pressure in cases of œsophageal eflux have already been described (Creamer 1955) After the carminative had been dministered, no change was observed in the ntragastric pressure in any case In those ases in which the carminative acted, the ressure changes of œsophageal reflux were bserved from five to fifteen minutes after dministration of the drug (fig 1) They ere identical with those recorded from atients with œsophageal reflux and occurred the same positions and with the same espiratory timing Often the reflux was ecorded with two or three respirations only nd it rarely lasted for longer than five inutes. Whether gas or fluid was refluxed epended on the position of the subjects, d the œsophageal reaction was the same that previously described The results of ese experiments are summarised in the ccompanying table

The changes of reflux were found in 9 of 10 healthy ople The one person who gave a negative result clared that she had never noticed eructation in her life

ULTS OF MEASUREMENT OF INTRA-ŒSOPHAGEAL PRESSURE AFTER ADMINISTRATION OF CARMINATIVES

| Cases | No | Reflux | No change |
|---|---|---|---|
| lthy people | 10 | 9 | 1 |
| ophageal muscular atrophy | 2 | 2 | |
| tric mucosal atrophy | 2 | | 2 |
| apetent hiatus hernia | 1 | 1 | |
| ysed left diaphragm | 1 | | 1 |

One patient with a hiatus hernia but without reflux s given carminatives and produced the changes of lux in exactly the same way as the healthy people e patient with paralysis of the left diaphragm showed change after carminatives and said that eructation d ceased since the onset of the paralysis This is of erest because reflux takes place only during inspiration d is probably precipitated by the changing shape of the ctum with the descending diaphragm.

2 patients with œsophageal atrophy due to scleroderma firmed by barium and pressure studies (Dornhorst al. 1954b) reacted normally to carminatives with ux, which fact suggests that the œsophageal muscle ys no part in the reflux mechanism. 2 patients with stric mucosal atrophy due to pernicious anæmia did t react to carminatives and 2 further patients with rnicious anæmia who were given carminatives without essure recordings did not belch Moreover patients th pernicious anæmia do not have the sensation of tension after carminatives.

*stroscopic Observations*

3 cases in which the local anæsthesia consisted in aying the throat only with 2% lignocaine showed ite mucosal changes after the introduction of minatives After five minutes the area around the ng juice became a deeper red and the rugæ became re prominent and the surface granular owing to an rease in size of the gastric areas No movements of e rugæ were seen Of 3 other patients who were æsthetised by sucking amethocaine tablets and allowing the juice, which presumably anæsthetises the stric mucosa, 2 showed milder changes and the 3rd none

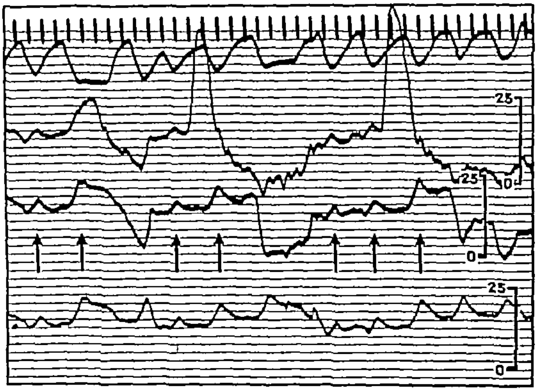

Fig 1—Recording from healthy person ten minutes after taking carminative : uppermost trace pneumogram (inspiration downwards) ; lower three traces, recordings from tubes 5 cm. apart (top two tubes in œsophagus and bottom tube in stomach) ; arrows reflux waves. Two propulsive waves are initiated by *presence of refluxed fluid in œsophagus.*

These observations show that carminatives cause hyperæmia of the gastric mucosa and the lesser reaction after local anæsthesia of the mucosa suggests that it is partly mediated through an axon reflex This action is not surprising because many carminatives are mild counter irritants, and some oils in the same group, such as turpentine possess strong rubifacient properties

## Discussion

### *Action of Carminatives*

Previous work on the action of carminatives has been focused on motility studies (Gunn 1920, Plant 1920, Plant and Miller 1926) which showed that carminatives

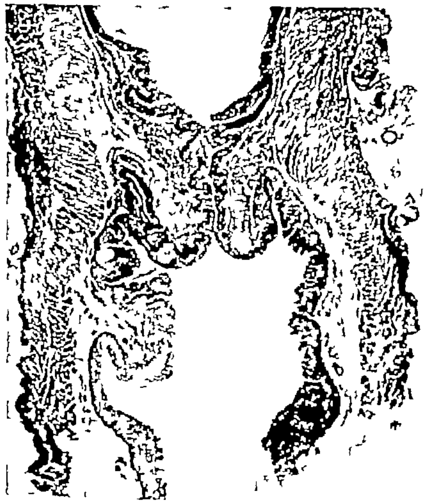

Fig. 2—Section of cardiac area of specimen showing mucosal

decreased motility and "tone" of the stomach in laboratory animals From this it was deduced that the "cardiac sphincter" was relaxed and eructation took place

The mechanism of the normal cardia has been investigated by Dornhorst et al (1954a), who show that the cardia is guarded by a valve The only structure capable of forming a valve in this area is the gastric mucosa, which appears to be drawn together by the muscularis mucosæ in a purse string manner, moreover the muscularis mucosæ is thickened in this area (fig 2) These workers showed that participation by extragastric structures was unnecessary for the competence of the cardia, and it is well known that there is no anatomical evidence of a sphincter

There are two components of this valve on which carminatives could have an effect—the mucosa and the muscularis mucosæ The gastroscopic observations show that carminatives cause hyperæmia of the gastric mucosa This change must increase the thickness of the mucosa and make it more turgid Any decrease in the mobility of the mucosa about the cardia will hinder the neat apposition of mucosal folds to form the valve

Little is known of the behaviour of the muscularis mucosæ, but the observations on patients with the gastric atrophy of pernicious anæmia suggest that it plays little part in the action of carminatives In spite of mucosal and muscular atrophy the muscularis mucosæ appears normal at the cardia in this condition (H A Magnus, personal communication) The failure of carminatives to act in these cases suggests that the mucosa is at fault and, owing to atrophy, cannot become sufficiently hyperæmic to affect the valve mechanism

Carminatives must therefore act on the cardia by altering the mucosal pliability, with the result that, with the changing shape of the cardia on posture and inspiration, the valve occasionally opens and allows reflux

### *Œsophageal Reflux*

These observations on the action of carminatives show one way in which the cardia can be rendered incompetent It is reasonable to suggest that this mechanism underlies reflux from other causes Essentially it depends on a change of the physical characteristics of gastric mucosa making it less pliable This may be hyperæmia, as in the case of carminatives, an increase in the number of mucosal cells, as in hypersecretion, infiltration of the mucosa with inflammatory exudate, as in gastritis, or infiltration with neoplastic tissue Minor degrees of reflux are common after a meal, and this can be reasonably attributed to hyperæmia of the mucosa A large proportion of cases of hiatus hernia with reflux have increased gastric secretion (Belsey 1952), and here the increased thickness of the mucosa may be a contributory factor in opening the cardia Eructation is a prominent symptom in the syndrome of chronic atrophic gastritis, where inflammatory exudate and increased collagen alter the mucosa, as opposed to the gastric atrophy of pernicious anæmia, where there is no inflammatory exudate The scanty gastric secretion in this condition probably prevents œsophagitis Finally, reflux is commonly found with neoplasms infiltrating the mucosa about the cardia

## Summary

Recordings of intra-œsophageal and intragastric pressures show that carminatives cause œsophageal reflux similar to that in pathological states

Gastroscopic observations reveal that carminatives cause hyperæmia of the gastric mucosa, and evidence is produced that the effect on the muscularis mucosæ is insignificant

This mucosal hyperæmia must interfere with neat [illegible] mucosal valve and allow reflux

This mechanism may underlie other states of reflux where the pliability of the mucosa is decreased from other causes

I wish to thank Mr R W Halls and Mr M G Venton for technical assistance, Dr R H Thomlinson for permissio to publish fig 2, and Mr A E Clark for the photograph.

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# EFFECT OF PIPERAZINE DERIVATIVES ON CERTAIN INTESTINAL HELMINTHS

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A SURVEY undertaken to ascertain the incidence roundworm and hookworm infestation of children certain coastal areas of New South Wales led to effort to find methods of treatment less toxic and diffic than those in vogue that might safely be used in routi mass therapy

## Investigation

The drugs tested were diethylcarbamazine (dieth carbamyl methyl piperazine dihydrogen citrate, 'Hetr zan,' 'Banocide'), piperazine hydrate ('Antipar'), a piperazine adipate ('Entacyl')

The patients were children aged from 1 to 14 yea and the *tests for ova were made by the* salt flotati method

The highest egg-counts before treatment were asca 153,000, necator 54,000, and trichocephalus 13,000 p g of fæces

## Results

The results obtained with *Ascaris lumbricoides* a *Trichocephalus dispar* are set out in the accompanyi table

*Necator americanus*—41 children treated with dieth carbamazine, 28 with piperazine hydrate, and 7 wi piperazine adipate showed no change in egg-counts.

*Hymenolepis nana*—4 children treated with piperaz adipate were unaffected

In the cases not cured by piperazine adipate the o of both ascaris and trichocephalus were extremely scan after treatment

RESULTS OF TREATMENT

| Drug | Daily dose (mg) | Duration of treatment (days) | No of children treated | No. o childre ova fr 2½ we after treatm |
|---|---|---|---|---|
| *Ascaris lumbricoides* | | | | |
| Diethyl carbamazine | 13 per kg of body weight | 3 | 54 | 12 (22 |
| Piperazine hydrate | 75 per kg of body weight | 3 | 26 | 20 (77 |
| Piperazine adipate | 300 per yr of age (max. 1800 [about 75 per kg of body weight]) | 3 | 47 | 45 (96 |
| *Trichocephalus dispar (Trichuris trichiura)* | | | | |
| Piperazine hydrate | 75 per kg of body weight | 3 | 22 | 4 (18 |
| Piperazine adipate | 300 per yr of age (max 1800) | 3 | 31 | 28 (90 |

The maximum number of ascarids passed was 50

Children treated with the soluble hydrate passed most of their worms early on the second day of treatment, whereas with the more insoluble adipate their evacuation extended to the third and even fourth day and in multiple infestations trichocephalus was voided earlier than ascaris.

No toxic or unpleasant reactions occurred except with diethylcarbamazine, which was too toxic to give in effective dosage.

The daily dose in every case was given as a single dose and not divided as recommended by the manufacturers. No aperients were given

Some children with ascariasis were given trial daily doses of piperazine hydrate 25–55 mg per kg of body weight over one two or three days The results were very variable: a single dose of 25 mg per kg of body weight was sufficient in some cases to cause disappearance of ova whereas in others this amount was quite ineffective Factors such as amount of food intake may have affected the result

## Comments

The results of treatment show that diethylcarbamazine is unsatisfactory in the treatment of ascariasis

Piperazine hydrate is effective against ascaris in a large proportion of cases but not against trichocephalus whereas piperazine adipate has the advantage of being most effective against both ascaris and trichocephalus —the latter a parasite found resistant to older forms of treatment.

The absence of toxic reactions suggests that further trials may show that more massive and fewer doses will be both safe and effective

Regulation of food intake or premedication may also enhance the action of piperazine adipate

Further investigation is being undertaken

# THROMBOCYTOPENIA DUE TO PLATELET AGGLUTININS IN THE NEWBORN

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The antibody mechanism of some secondary thrombocytopenias is well known—e g purpura due to Sedormid (Ackroyd 1949) and to quinidine (Broch 1941 Sekelman et al. 1948 Norcross 1950 Hirsch and Dameshek 1950 Collins 1950 Larson 1953) Since the report published by Evans et al (1951) several workers have brought forward facts suggesting an antibody mechanism in some of the so called idiopathic thrombocytopenias but there was no definite proof before anti-platelet agglutinins were shown to exist

There are many objections to the earlier techniques devised to demonstrate platelet-destroying factors. All of them are based on the agglutination of healthy platelets which have been lysed by contact with an unknown serum. The main difficulties are the tendency of thrombocytes to agglutinate spontaneously and the fact that the combination of serum and thrombocytes may in some instances liberate thrombin which in turn produces clotting Many precautions are therefore necessary, these we have discussed elsewhere (Verstraete and Vandenbroucke 1955)

## Methods

Besides the direct method, one can use the indirect Coombs test or human anti platelet serum (Moltheniu et al 1953) or a modification of the Middlebrook Dubos hæmo agglutination method (Kissmeyer Nielsen 1953) We used the first and the last of these methods in a case of thrombocytopenia

The principle of the Kissmeyer Nielsen method is the fixation of the antigen by the red blood cells (the platelet extract being the antigen in the present case)

*Reagents*

The red cells are first preactivated to facilitate the adsorption of proteins on their surface as follows:

A 2% suspension of group-O red cells in buffered saline solution (pH 7 2) is incubated at room temperature for 10 minutes with an equal volume of a freshly prepared tannic acid solution (1/40 000 in saline solution) The red cells are next washed in buffered saline serum of pH 7 2 and brought again to a 2% suspension in saline solution (0·85 g NaCl%)

The platelet extract is prepared as follows

The platelets are precipitated by fractional centrifugation of citrated healthy plasma They are next suspended in saline solution (about 600 000 per c.mm.) and frozen at −4°C and defrosted several times. After centrifugation the supernatant liquid is decanted and preserved as the platelet extract

The suspension of red cells is added to the buffered (pH 6 5) platelet extract (vol 1 1) and left at room temperature for 10 minutes The red cells are next separated by centrifugation, washed twice with a mixture of saline solution and 1% or 2% human serum, and suspended in the same liquid to make a 1% suspension A little serum is added to prevent hæmolysis

*The Test*

A known amount of the serum to be tested (or an aliquot if the titre has to be determined) is mixed with the same quantity volume for volume of sensitised red cells in a series of hæmolysis-tubes The tubes are then shaken for 30 minutes and examined for agglutination at the end of 2 hours and 24 hours. If hæmo-agglutination has taken place, the test is positive

## Case report

A young mother aged 27, had bled easily since childhood but never seriously enough to require medical attention, and she had borne three children without undue trouble Spontaneous ecchymoses began to appear in 1951 but were not given any serious thought until May 1953 when long continued epistaxis led her to consult a doctor

*On examination* she was two months pregnant and otherwise healthy except for slight anæmia. No glands were palpable, and the spleen and the liver were of normal size A blood-count showed Hb 80% red cells 3 600 000 per c.mm., white cells 10 800 per c.mm. (neutrophils 55%, eosinophils 3% basophils 0 lymphocytes 36% monocytes 6%) The erythrocyte-sedimentation rate was normal. The plasma bilirubin level was 0·6 mg. per 100 ml and bleeding time 6 min. There were 46,800 platelets per c.mm. Bone marrow showed a normal distribution of blood elements, young and adult megakaryocytes in particular being present in normal proportions.

*Operation.*—Because of the severe thrombocytopenia and the increasing hæmorrhages splenectomy was done to avoid accidents at parturition. A normal spleen was removed in October 1953 no accessory spleens being found A few days after the splenectomy the number of platelets increased to 300 000 per c.mm

*Parturition*—A baby weighing 7 lb was born two months later delivery being uneventful. The baby was healthy except for numerous petechiæ all over the body No enlargement of lymph nodes, spleen or liver was found A blood count showed Hb 115%, and red cells 5 000 000 per c.mm The subsequent hæmatological history of mother and child is given in the accompanying table and figure.

*Tests*—On Jan. 11 1954 we found by the direct method anti platelet agglutinins in the serum of both mother and baby On Feb 19 1954 agglutinins were still present in the mother's serum but no longer in the baby's (Kissmeyer Nielsen test) Both mother and baby belong to blood group O CeDe RIK, and in February 1954 there was no evidence of anti polymorph agglutinins or of iso-agglutinins. The

HÆMATOLOGICAL HISTORY OF MOTHER AND CHILD

| Date | Mother | | | | Child | | | |
|---|---|---|---|---|---|---|---|---|
| | Platelets (per c mm ) | Bleeding time (min ) | Purpura | Clot retraction | Platelets (per c mm.) | Bleeding time (min.) | Purpura | Clot retraction |
| May 28 1953 | 46,800 | 6 | + + + | | | | | |
| June 10, 1953 | 58,000 | 11 | | | | | | |
| July 11 1953 | 3500 | 30 + | + + + + | Insufficient | | | | |
| Oct 3, 1953 | 7000–10 000 | | | | | | | |
| Nov 4, 1953 | 196 000 | | | | | | | |
| Dec 3, 1953 | 280,000 | | - | | 10,000 | 22 | + + + + | Absent |
| Dec 12 1953 | | | | | 6000 | | | |
| Dec 14, 1953 | | | | | 7000 | 1½ | Nil | Light |
| Dec 17, 1953 | 80 000 | | | | 17,000 | 1¼ | Nil | |
| Jan 11, 1954 | 144,000 | | Nil | | 100,000 | | Nil | Nil |
| Feb 19, 1954 | 288,000 | 1¼ | Nil | | 110,000 | | | |
| March 16, 1954 | 110,000 | | Nil | | 260,000 | 1½ | | |

Coombs test was negative in the serum of both mother and baby *

*Follow up* —The purpura disappeared spontaneously and completely in the baby after six or seven days, and all further blood examinations were normal

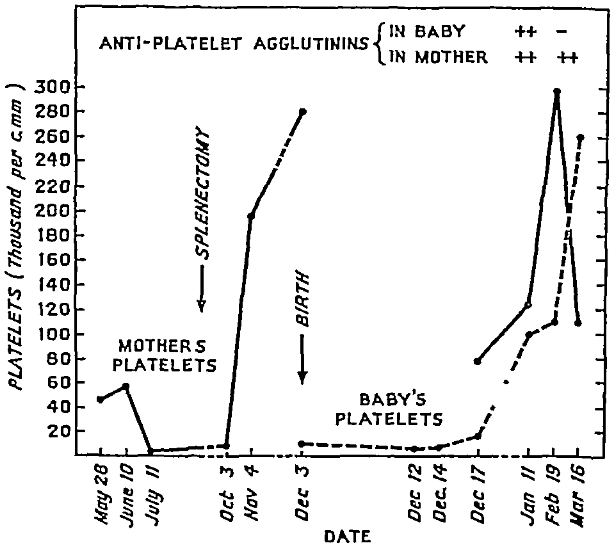
## Discussion

Since 1924 thrombocytopenia purpura in the newborn has been reported at intervals In all the published cases the baby was born with purpura, which faded gradually in the first days of life Landolt (1948) differentiated between three groups of congenital purpura, of which the first two disappear spontaneously (1) the more important affects children born of mothers who have either Werlhof's disease (thrombocytopenic purpura) or secondary purpura, and (2) purpura affecting babies whose mothers had no hæmorrhagic disease

Robson and Walker (1951) published an unusual case in which the mother was healthy at the time of the birth but started having hæmorrhagic manifestations three weeks after giving birth to a baby with generalised purpura, only then did the undiagnosed Werlhof's disease of the mother become obvious

A third group of thrombocytopenia, often lasting a long time, is due to congenital hypoplasia of the megakaryocytes

Our observation is of interest because of the presence of anti-platelet agglutinins in the serum of both the mother and her baby—a finding which has not previously been published These agglutinins disappear spontaneously from the baby but persist in the mother Th anti-platelet agglutinins can continue to be formed an pass through the placental barrier even after splenectomy



and anti platelet agglutinins in mother and baby

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* We are indebted to Dr J J Van Loghem and Dr A J Sauer Amsterdam for their help in controlling the antibody reactions

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# SODIUM-NITRITE POISONING TREATED BY EXCHANGE TRANSFUSION

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Sodium nitrite is an exceedingly deadly poison, and a products containing it should be marked prominently such, and at least an approximate formula should b given of their contents Machine oil containing sodium nitrite is increasingly used and is widely obtainable fro engineering firms

## Case-record

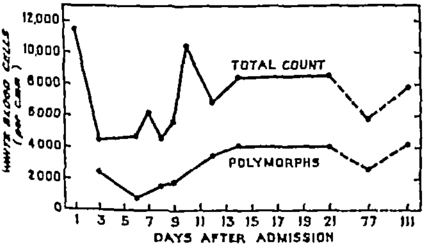
A girl, aged 11, was admitted on May 28, 1954, fifty minute after having taken one mouthful of an unknown machine-oi some of which she spat out A sample of this oil was brough along, but attempts to obtain the formula from the work where it was being used and the dealers from whom it wa bought were unsuccessful

*On admission* the patient was unconscious, pale, an extremely cyanosed Her pulse and respirations were feebl and she did not respond to painful stimuli When intravenou nikethamide 3 ml was given, the venous blood was seen t be thick and chocolate brown, methæmoglobinæmia wa diagnosed In view of this and of the patient's rapid deteriora tion a replacement blood transfusion was started

*Treatment and Progress* —While the anæsthetist administere oxygen and did gastric lavage, an intravenous transfusio was started of group O Rh negative blood which was not cross matched until later The median cubital vein was opened fo venesection, but rapid clotting made this very difficult T hasten the withdrawal of blood the radial artery was partially divided at the wrist Rapid clotting persisted until about 1250 ml of blood had been transfused, it was so rapid that a nurse had to keep wiping away clots to maintain blood flow from both vein and artery When 1000 ml of blood had been transfused and the patient's condition had begun to improve, hirty to forty minutes after admission, the West Midland Forensic Science Laboratory to which a sample of the oil ad been sent, reported that it contained 30 5% of sodium nitrite 7·5% of an emulsifying agent and 56·0% of water Sodium nitrite 7–8 mg per 100 ml was present in the stomach washings. Spectroscopy showed methæmoglobinæmia Altogether 1700 ml. of blood was transfused. The patient was nursed in an oxygen tent for forty-eight hours. Pyrexia and increased pulse-rate persisted for four days Radiography of the chest showed no abnormality The urine was normal. Procaine benzylpenicillin 300 000 units twice daily and ascorbic acid 300 mg daily were started on admission and continued for twelve days.

*Examination of the blood* next day showed normal oxyhæmoglobin and Hb 15 g per 100 ml. The following day the Hb was 17 4 g per 100 ml. A white-cell count showed granulocytopenia (see figure) the polymorphs decreasing from 51% on May 31 to 19% on June 3 and was not normal until June 7 —i.e., the tenth day Türk s cells and toxic granules in the polymorphs were present on June 3 but not afterwards On June 11 the blood picture including absolute values was within normal limits and the patient was discharged fourteen days after the accident

*Follow up*.—On June 18 a white-cell count showed 8300 per c.mm. (metamyelocytes 1% polymorphs 50 5%) Eleven weeks after admission the blood picture was normal with Hb 14 1 g. per 100 ml. white cells 6000 per c.mm. (polymorphs 44%) The child looked well and had been normally active after a fortnight s convalescence Sixteen weeks after admission her blood picture remained normal with Hb 14 7 g per 100 ml. and white cells 8000 per c.mm. (polymorphs 54%)



White-cell counts.

### Discussion

Sodium nitrite is absorbed rapidly its effects starting five to twenty minutes after ingestion Absorption starts sublingually causing vasodilatation and, in large doses syncope and methæmoglobinæmia The methæmoglobin is the stable oxidised form of hæmoglobin with the iron in the trivalent ferric state This form is only slowly broken down in the body and thus is of little value in supplying oxygen to the tissues There is also a shift of the oxygen dissociation-curve to the left making the oxygen less readily available to the tissues

Ascorbic acid in doses of about 500 mg daily is of value in the chronic mild cyanotic case but severe cases of either chronic or acute methæmoglobinæmia require more rapid action Intravenous methylene blue 1–2 mg. per kg of body weight is reported to be effective in the methæmoglobinæmia following ingestion of nitrites in drinking water by infants but in acute poisoning with a moribund patient it is quicker and more satisfactory to start an exchange transfusion The removal of the methæmoglobin together with any nitrite still circulating and the substitution of transfused blood will lessen the degree of bone-marrow damage with the resulting neutropenia. No time should be wasted in waiting for experts in exchange transfusion the doctor who first sees the patient should give it

### Conclusion

In severe cases of sodium nitrite poisoning an immediate exchange transfusion may be life-saving and is the method of choice

Prolonged observation of the case is subsequently needed because of the danger of neutropenia and agranulocytosis despite a good general clinical condition, which is misleading

*I wish to thank Mr J S Horn for permission to publish Mr Roscoe Clarke for advice and encouragement; Dr S, Sevitt for hæmatological reports and Prof T M Webster of the West Midland Forensic Science Laboratory for the speedy analysis of the mixture and for advice about after treatment*

# RUPTURE OF THE DUODENAL STUMP AFTER GASTRECTOMY

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Polya gastrectomy is one of the commonest major operations The risks associated with it have considerably diminished in the last fifteen years but still a few of the patients die and one of the commonest causes of death is rupture of the duodenal stump For this reason many methods of closing the stump have been devised

In some cases in which leakage subsequently takes place the duodenum has been difficult to close (e g, in patients with an adherent ulcer of the posterior duodenal wall); but in others, leakage follows a simple straightforward operation in which no difficulty whatever was experienced in closing the duodenal stump apparently securely This state is almost invariably the sequel to operations for gastric ulcer or for malignant disease, when the duodenal stump occasionally ruptures In such cases the rupture is often attributed to an inability of the patient's tissues to heal, and malnutrition is blamed but in many of these cases no disorder of nutrition or imbalance of fluid or electrolytes can be found

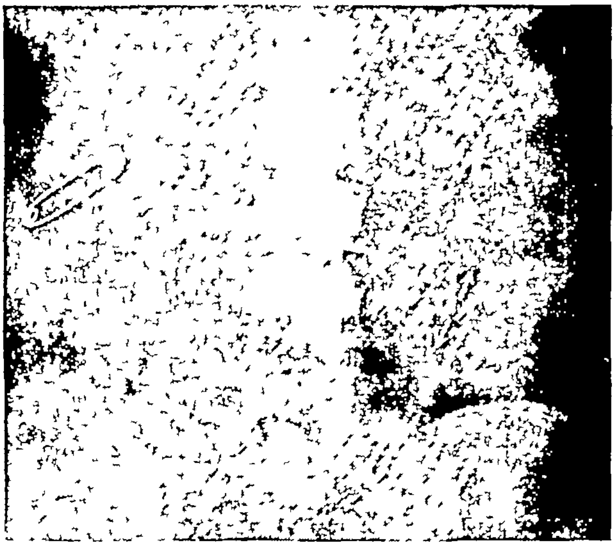
Aird (1949) Wangensteen (1941), and Tanner (1954) have emphasised that distension of the duodenal stump due to obstruction of the afferent jejunal loop may be the most important factor in rupture of the duodenal stump in such cases Usually after leakage it is difficult at operation to be certain about pre existing distension of the afferent loop The following case is reported because there was clinical evidence of such a derangement and it was clearly confirmed at operation, the afferent loop with the duodenal stump being distended virtually to the point of rupture of the stump

### Case report

A married woman aged 37 was admitted to Paddington General Hospital with a history of ten years typical duodenal dyspepsia and one previous attack of melæna She had already undergone medical treatment with temporary benefit, but her symptoms had now recurred

*On examination she* was rather pale but otherwise looked fit and no abnormality was detected on ordinary clinical examination Further investigation however showed moderate anæmia and radiological evidence of a posterior wall duodenal ulcer After correction of her anæmia she was operated on

*Operation.*—The abdomen was opened through an upper right paramedian incision and the presence of free confirmed Without undue difficulty a high partial of the Polya-Hofmeister Finsterer type was abdomen was closed with stab drainage down the closed duodenal stump because this perfect



**Radiograph showing distended afferent jejunal loop in left side of abdomen six days after Polya gastrectomy**

*Progress* —Immediately postoperatively the patient's condition was satisfactory Intermittent gastric suction through an indwelling Ryle's tube was used, and fluids were administered intravenously Oral fluids were gradually instituted, but the Ryle's tube was left in situ for the purpose of an occasional aspiration to prevent overdistension of the gastric remnant It was finally removed on the fourth postoperative day, when the last aspirated fluid contained bile and the afferent loop was therefore presumed to be patent The patient's condition was excellent and remained so for a further two days, when she started to complain of colicky abdominal pain not associated with vomiting She looked rather anxious, and her pulse rate was raised Examination of her abdomen revealed no generalised distension, but in the left upper quadrant a tender resonant localised swelling was just palpable No relief of symptoms followed an enema, which produced a normal result with the passage of fæces and flatus, and the abdominal swelling was still palpable and unchanged A straight radiograph of the abdomen (see figure) showed a gas distended loop of bowel in which valvulæ conniventes could just be detected In the absence of vomiting obstruction of the afferent loop was diagnosed

*Second Operation* —On laparotomy the duodenal stump was found to be intact but, together with the afferent loop, grossly distended The obstruction appeared to be at the valve and due to occlusion of the jejunum from without by the closed portion of the cut end of the gastric remnant The efferent loop was normal in calibre, the stoma between it and the gastric remnant being patent An entero anastomosis was effected between the afferent and efferent loops, and the abdomen was closed

*Subsequent Progress* —Parenteral fluids and gastric suction were reinstituted for a few days, after which the patient made an uneventful recovery and was in due course discharged When last seen in the follow up clinic she was feeling well and appeared normal on examination

## Discussion

It seems likely that, unrelieved, the obstruction would have proceeded to perforation of the duodenal stump, and that timely surgery obviated a serious catastrophe If distension of the afferent loop is often a factor in causing leakage from the duodenal stump, it would be gratifying indeed if it could always be recognised at this stage

Clearly diagnosis of obstruction of the afferent loop would be aided if it was associated with some definite syndrome In the present case the picture presented was sufficiently definite to enable such a diagnosis to be made The presence of an isolated distended coil of bowel clinically palpable in a patient exhibiting colicky abd pain, without vomiting, constipation, or generalised abdominal distension, strongly suggested the condition Radiological examination lent considerable support to this clinical impression

Retrospective examination of the notes of eight cases of duodenal leakage showed that, with the exception of one early rupture associated with inadequate closure, all the patients exhibited slight but definite signs suggesting some preliminary disorder before actual leakage began The number of cases is small, but the findings conform with the commonly held view that even before rupture the postoperative progress of such patients is rarely smooth The clinical features did not, apparently, form such a well-defined picture as in the present case, the most constant finding between operation and leakage being abdominal pain or discomfort associated with a raised pulse-rate There was no record of radiography of the abdomen save in one case, where the generalised bowel distension was probably a manifestation of the ileus accompanying an already ruptured duodenal stump

## Conclusions

It seems likely that many cases of rupture of the duodenal stump after gastrectomy are preceded by prodromal symptoms and signs possibly related to obstruction of the afferent loop The diagnosis of this condition would be greatly facilitated by the demonstration clinically or radiologically of the distended loop The suggestion is therefore made that all cases after Polya gastrectomy where the cause of unsatisfactory progress is not evident not only should be submitted to careful abdominal palpation for localised distension but also should undergo routine and early radiological examination of the abdomen In this way more cases of obstruction of the afferent loop may emerge, and the incidence of duodenal leakage be lowered by timely surgical intervention

I wish to thank Prof J C Goligher for permission to publish, and the photographic department at St Mary's Hospital, London, for the photograph

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# SUPPRESSION OF URINE IN ASPIRIN POISONING

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M D Lond, M R C P
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Patients undergoing full salicylate therapy have often been reported to have albumin, red cells, and casts in their urine Krasnoff and Bernstein (1947) and Biddle (1938) described glomeruli congested with red cells and tubular degeneration and necrosis in fatal poisoning, and Scott and Hanzlik (1916) and Hanzlik and Karsner (1917) described similar lesions in dogs and cats after large doses of salicylates Gross and Greenberg (1948) considered that salicylates in amounts sufficient to produce poisoning might cause nephritis

Only a few reports have been published which mention a diminished urinary output in salicylate poisoning, a development which should profoundly modify the treatment Andrews (1938) described oliguria in one case and Charters (1944) in two others Scott et al (1917) recorded considerable diminution in urinary output after the administration of full therapeutic doses of salicylates, it reached its maximum about 10–20 hours after the symptoms of "toxicity" appeared, and returned to normal shortly before, or about the time that, the excretion of salicylate was completed

A case of severe salicylate poisoning with almost mplete suppression of urine is described here

### Case-report

A woman, aged 57 was admitted under the care of Dr L C rtin on Oct 4 1954 in deep coma with rapid deep respira n, flushed, and sweating profusely Her temperature was 1·6°F pulse-rate 120 blood pressure 180/120 mm Hg ne acid, with sp gr 1 010 a trace of protein, and salicylates ++ It was established later that she had taken acetyl icylic acid gr 250–300 (50–60 aspirin tablets) the previous ening.

*Treatment and Progress* —She was treated for salicylate soning by gastric lavage large amounts of intravenous d (170 oz. of N/5 saline solution with 4% dextrose in the t 24 hours) 7 oz. of 5% sodium bicarbonate (discontinued en the urine became neutral) vitamin K 100 mg 8 hourly travenously penicillin and pharyngeal suction and oxygen necessary In spite of this the patient s condition deterior ed during the first 8 hours with pulse rate rising to 140 mperature 103 4 F and blood pressure falling to 120/80 mm g In the first 12 hours after admission the urinary output s 75 oz. Pulse-rate and respiration rate had improved and e temperature was lower by the following morning The tient was no longer in coma but became maniacal and quired paraldehyde In other respects her condition was satisfactory Her blood pressure had fallen to 100/65 mm. g at 7 A.M and to 80/60 mm. Hg at 8 A.M ; this was restored 130/85 mm. Hg 4 hours later after 20 oz of plasma had been ven. The patient had numerous fits during the morning d was given more paraldehyde She did not recover nsciousness again until 24 hours later

*Suppression of Urine* —In the second 12 hours the urinary tput was only 3½ oz. in spite of copious intravenous fluids. e urine contained protein red cells, and hyaline and anular casts. In view of the extreme oliguria intravenous ids were discontinued 27 hours after admission On the llowing days treatment for anuria was given as described y Bull et al (1949) and was continued until adequate ounts of urine were passed a high carbohydrate low otein diet was then substituted for it The patient felt well d was fully conscious by the 4th day

The urinary volumes were as follows

| | | | | |
|---|---|---|---|---|
| 1st day | midday to midnight | 75 | oz. | |
| 2nd day | midnight to midday | 3½ | oz | |
| " " | midday to midnight | 9 | oz | |
| 3rd day | midnight to midday | 3 | oz | |
| " " | midday to midnight | 6 | oz | |
| 4th day | 24 hr | 18 | oz | (urine + semi-solid stool) |
| 5th day | " | 114 | oz | + |
| 6th day | | 34 | oz. | |
| 7th day | | 44 | oz | |

The concentration of urea in the 24 hour specimens of ine gradually increased from 0·49 g per 100 ml on the d day to 1 8 g per 100 ml. by the 8th day Red cells and sts disappeared from the urinary deposit by the 5th day d the blood urea level which had reached a peak of 177 mg r 100 ml. on the 5th day had fallen to 33 mg by the 10th ay Salicylates had disappeared from the urine by the 7th ay

### Discussion

It has been suggested that the oliguria associated with licylate poisoning might be due to dehydration caused y excessive sweating (Scott and Hanzlik 1916) but is was not the cause in the present case the urine being ute, with sp gr 1 010 and the urea level low It erefore seems that the suppression of urine was prob bly due to renal damage which is known to occur in licylate poisoning It is very unlikely that this renal volvement was due to the extremely transient hypo nsion which was neither sufficiently severe nor fficiently prolonged to cause tubular necrosis A direct phrotoxic action of salicylates seems to be a more kely cause

In a case such as this it is evident that the usual eatment of salicylate poisoning with copious intra nous fluids and alkalis might well prove fatal if ntinued after the development of severe oliguria Pulmonary œdema has, in fact, been reported several times in fatal cases of salicylate poisoning and may possibly have been due to overhydration

### Summary

A woman, aged 57, with salicylate poisoning developed extreme oliguria She was given the usual treatment for acute renal failure and recovered

I wish to thank Dr L. C Martin for his advice and per mission to publish, and Dr Paul Fourman for his help in the preparation of this paper

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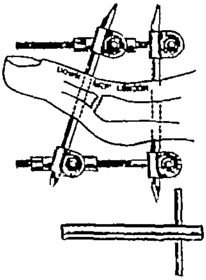
## New Inventions

### COMPRESSION CLAMP FOR ARTHRODESIS OF FIRST METATARSO PHALANGEAL JOINT

ARTHRODESIS of the first metatarso-phalangeal joint has been advocated for selected cases of hallux rigidus and hallux valgus In order to shorten the time of immobilisa tion and to ensure more certain arthrodesis, an attempt has been made to apply the principle of compression arthrodesis to this joint

The problems involved are the fixing of the joint in flexion and slight adduction the transfixion of the bones on each side of the joint with Steinmann s pins without splitting the bone, the avoidance of a scar in this weight-bearing area, and the avoidance of injury to the tendons.



Messrs. Down Brothers have made for me a compression clamp which I think fulfils these requirements. It consists of two short Steinmann s pins which are fixed into two screw-clamps which have been modified from the East Grinstead fixation apparatus for the treatment of fractures of the jaws (see figure) The universal clamps of this apparatus enable the pins to be inserted at an angle instead of parallel

The first metatarso phalangeal joint is denuded of cartilage and the bone surfaces are cut to give the required flexion and adduction and exact apposition of the cancellous bone Before inserting the Steinmann's pins, the bones are drilled with a ⅛ *in. drill* in order to avoid splitting the bones The proximal pin is then passed downwards and slightly backwards, in order that the pin may come out through the skin behind the pressure-point of the ball of the great toe. The distal pin is passed vertically downwards—that is, obliquely through the flexed phalanx The clamps are then applied and screwed tight

It has been found that after three weeks there is firm clinical union, and the patient is allowed up walking after four weeks.

This instrument can be obtained from Messrs Down Bros. and Mayer & Phelps Ltd., 32, New Cavendish Street W 1

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# Reviews of Books

## Medical History of the Second World War

*The Royal Air Force Medical Services* Vol 1 Administration Editor Squadron Leader S C REXFORD WELCH, M A, M.R C S H.M Stationery Office 1954 Pp 611 70*s*

THE exact date of the birth of the Medical Branch of the R A.F seems uncertain, but its growth can hardly be said to have begun until after the end of the first world war, and it faced its first big test in 1939 unencumbered by too much experience To this absence of rigidity can be ascribed the successful development of activities which had not been foreseen Rehabilitation units and special departments for treating burns and facial injuries are examples of clinical work, fostered by a sympathetic administration to meet an immediate war-time need, which later diffused through the whole of medical practice Planning for the unknown is disappointing work, only made tolerable if a good deal of variation is allowed for It is in a way symbolic that of the general hospitals constructed by the R A F early in the war, the hutted buildings were found to be more easily altered to meet changing needs

Among the specified aims of this history is the definition of mistakes in the light of after-knowledge, and Squadron-Leader Rexford-Welch has recorded faithfully both success and failure His difficulty in selecting material must have been great, and the interest of the sections have a varying appeal The struggles and difficulties of organising the air transport service for the sick and injured are well described, and the description should be widely read, for there was much criticism at the time The story of the final achievement during the invasion of France is dramatically exciting Another chapter of general importance is that on medical man-power The fighting Services are usually held to be greedy in their demands for doctors here are set down the arguments and increases for all to see

Much of the volume, though of domestic interest to those who served in the R A F, carries no wider lessons Something shorter than three volumes at 70*s* each would probably be more welcome to outsiders

## The Casualty Department

T G LOWDEN, M A, B M, F.R C S, consultant surgeon, Sunderland Royal Infirmary Edinburgh and London E & S Livingstone 1955 Pp 278 37*s* 6*d*

THE casualty department is the shop window of a busy general hospital, yet it is sometimes neglected by the senior members of the staff Mr Lowden sets the work of the casualty department in proper perspective His book will be of value to everyone, from house-officer to consultant, who has anything to do with surgery, and it should be read by the medical student in his final year He combines good sense with clear exposition and excellent illustrations, and he deals with conditions that are common and of economic importance

Mr Lowden sees the problem of casualty work in the setting of our times He does not merely repeat descriptions of septic conditions and injury, and their treatment, he guides the reader in the management of the case and the situation The patient's financial and temperamental background occupies one chapter, sound advice on legal responsibilities another, and legal protection the next, in another the implications of industrial injury and disablement benefit are considered His appendices show the value of simple investigations conducted despite the hurly-burly of such a department. This is a valuable book

## The Graphomotor Projection Technique

*Clinical Use and Standardisation* SAMUEL B KUTASH, PH.D, chief, clinical psychology section, Veterans Administration Hospital, East Organge, New Jersey, RAYMOND H. GEHL, M D, psychiatric consultant, Newark regional office, mental hygiene clinic, Veterans Administration. Springfield Ill Charles C Thomas Oxford Blackwell Scientific Publications 1954 Pp 133 27*s* 6*d*

FOR assessing personality, drawings have the advantage provide permanent records of self-expression The difficulty is to know what they represent, and to compare them one with another Some people think they have only to look at a drawing to interpret it correctly, but the authors of this book hold that skill in classifying records can be developed only through practice and experience under the supervision of an 'indoctrinated and trained" examiner

The subject has no model to follow He is blindfolded during the entire graphomotor performance, and the "fundamental rule" is to ask him to move his pencil freely over the paper provided, and "to try not to make anything definite" The aim is to elicit free expression from inner promptings, and to note the character of such movements Each subject is later asked what he was thinking about while he was drawing, and, finally, whether he is able to recognise parts of what he drew The authors claim that this association part of their test is unique, being "loaded" by the subject himself, in the sense that he creates the material out of which content is first delineated, and then used as the stimulus for association.

Normative data consist of "200 well-substantiated schizophrenic patients" and a control group of "200 apparently normal persons" Since only these two groups are compared, the test's practical value cannot be assessed, however much we may admire its theoretical principles.

## Analgésie obstétricale

B JAMAIN, gynécologue accoucheur de l'Hôpital Tenon, R GIRAUD, assistant en obstétrique des Hôpitaux de Paris Paris Masson 1954 Pp 156 Fr 900

THIS is a fairly comprehensive work on the clinical aspects of obstetrical analgesia Pain in labour, its mechanism, and the practical implications of analgesia in terms of fœtal physiology are discussed, but the greater part of the text consists of descriptions of the drugs and techniques for relieving pain.

Perfect analgesia in childbirth is still an elusive ideal, and Dr Jamain and Dr Giraud rightly emphasise the need for clinicians to keep an open mind and select the method suited to the particular patient and obstetrical problem Their own views are similar to those widely held in this country, and they show a preference for general rather than local methods of analgesia

## Hospital Planning Requirements

GUY ALDIS, A.R I B A. London Pitman 1954 Pp 207 85*s*

Mr Aldis is the architect to the East Anglian Regiona Hospital Board, and his book is primarily for architects but it will also be useful to the many doctors who are likely to be concerned with hospital reconstruction in the coming years

He does not attempt to impose a standard design for future hospitals, but he sets out the basic needs for individual departments, and indicates the importance of correct lines of traffic and the needs of patients as well as of medical and nursing staff In short detailed notes supplemented by over 400 diagrams he covers the clinical service of a hospital—the casualty department, outpatient department, different ward units, operating-theatre, X-ray department, pathology department, and mortuary block In a later book he hopes to deal with the administrative and service departments

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**Diseases of the Skin** (4th ed Philadelphia and London W B Saunders 1954 Pp 877 65*s*)—Dr G C Andrew has brought the new edition of his popular textbook right up to the minute and has at the same time reduced the tota number of pages by 60—good evidence that out-of date matte has been ruthlessly cut Though this is a book for specialists it is not unsuited to the practitioners and students, being lucidly written and telling the reader in fair detail what to do by way of treatment Possibly the dangers of treating tuberculosis of the skin with vitamin D are over-emphasised The chapter on syphilis has rightly been retained, but Dr Andrews seems to pin all his faith on penicillin, and states that 'supplementary treatment with arsenic and bismuth does not increase the good results and is of no value" This does not conform with current British ideas or practice. Nevertheless, this is a good book, well presented, with plenty of good illustrations and adequate references

THE LANCET

LONDON SATURDAY, MARCH 19 1955

## Tuberculous Lesions after Chemotherapy

The changes in tuberculous lesions after treatment with streptomycin[1] may be summarised as follows there is absorption of non specific exudate (e g, in tuberculous bronchopneumonia, meningitis and the perifocal reaction[2]) diffuse fibrosis perhaps going on to hyalinisation takes place in miliary foci and in small follicles round larger lesions while larger lesions and necrotic foci undergo fibrous encapsulation, and walls of cavities become densely fibrous, sometimes with a smooth surface and formation of a lining epithelium These changes are found especially in more recent lesions, whereas old densely fibrosed foci are unaffected All these changes have been found also in untreated patients (though perhaps only in occasional lesions and hardly ever in all lesions at once) absorption of non specific exudate,[3] fibrosis of miliary lesions,[4] and healing of cavity walls[5] have all been noted in the natural course of the disease Thus the effect of streptomycin is antibacterial and not on the tissues, the drug enables regression to take place in all lesions at once, with contracting fibrosis of the actual lesion (especially if recent) and clearing of the tissues around In chronic cavities with extensive fibrosis around them, no great improvement can be expected from this treatment active parts may become quiescent, but after chemotherapy has been stopped any part may become active again, even after a course of streptomycin tubercle bacilli can be isolated from the caseous contents and walls of such chronic cavities Thus streptomycin gives rise to no specific changes This assessment is confirmed by the five year report[6] of the first Medical Research Council trial of streptomycin in pulmonary tuberculosis. At the end of five years 2 out of 52 controls, compared with 9 out of 55 streptomycin treated patients, had required no further treatment and there were more arrested and quiescent cases in the streptomycin than in the control series, yet after the initial streptomycin therapy both series had required about the same amount of further therapy and surgical (including collapse) treatment Combination of streptomycin with p aminosalicylic acid (P A S) produces the same fibrosis in recent lesions with clearing of non specific exudate **Auerbach**[7] claims that treated lesions can be distinguished from untreated lesions by reason of the more rapid clearing of the perifocal reaction, but **Dick**[8] foun chronic renal lesions after three months' tre was impossible to decide how much of the osis was the result of treatment and how much was due to natural regression before treatment had been started

**Mackaness**[9] and **Suter**[10] have shown that isoniazid has a more powerful bactericidal action than streptomycin and that it kills intracellular as well as extracellular bacilli Corresponding histological changes have been reported In lung lesions **Panà** et al[11] noted congestion and increased vascularity in cavity walls with hæmorrhages into caseated material and around nodules not yet ulcerated, and also thinning and desquamation of the necrotic material **Berblinger**[12] found some healing in caseous and productive foci, with congestion and hæmorrhages, and his illustrations show desquamation of tuberculous granulation tissue and disappearance of epithelioid cells, and also absorption of non specific exudate **Könn**[13] reported that cavities to which isoniazid was applied locally by Monaldi drainage became lined with non-specific granulation tissue covered by stratified epithelium Similar changes were found in tuberculous kidneys[14] but the dense fibrosis which develops in and around lesions after streptomycin did not follow administration of isoniazid These changes followed treatment with isoniazid alone and were found in what would now be regarded as the early stages of treatment (the first three months) **De Figueiredo** and **De Paola**[15] suggest that the changes characteristically resulting from treatment with isoniazid are hyperæmia (commonly with small hæmorrhages) round all types of tuberculous lesions epithelial proliferation in bronchioles and lining alveoli, complete healing of cavity walls, sometimes with small stretches of lining cells many pleomorphic giant cells, patches of foam cells and exuberant collagenous formation **Denst**[16] had already drawn attention to the numerous atypical giant-cells, the patches of foam cells, and the surprising amount of non necrotic fibroblastic granulation tissue and he also remarked on the liquefaction of cavity contents with polymorphs and red blood cells though noting that this softening could take place spontaneously in untreated tuberculosis **Canetti**[17] described the disappearance of a large number of miliary tubercles, resorption of perifocal inflammation and fibrous or fibrohyaline transformation of persisting lesions, and he and others[18 19] have described the possible improvements in cavity walls **Dick**[14] ascribed these changes in recent lesions to resolution brought about by isoniazid in a way which there is no opportunity of observing in man but which has been described for miliary lesions in the liver, spleen and bone marrow of rabbits[20] There is much radiographic and clinical evidence to support the finding that recent lesions clear up completely after isoniazid therapy We have accordingly good grounds for hoping to find that in the five-year reports of the M R C trials of isoniazid a substantial proportion of patients have required no further treatment after combinations including isoniazid

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In chronic cavities and other chronic lesions, the resolution is modified by dense fibrosis and caseation [8] After changes in recent lesions have proceeded as far as the natural fibrosis allows there is nothing to distinguish treated from untreated lesions which have become quiescent naturally But bacteriological studies show that tubercle bacilli can be cultured from a large proportion of lesions in surgical specimens after chemotherapy Even if such specimens are negative to ordinary methods of culture, special methods [21] still demonstrate that many are positive Hence in these late cases chemotherapy alone does not suffice Despite the great advance in the treatment of tuberculosis by the introduction of these drugs, we must still concentrate on finding cases as early as possible and on initiating treatment without delay

## A Shared Responsibility

THE old, it is often said, are like children, and the temptation to treat them like children—to relieve them of all responsibility, manage their affairs, smile at their protests, and chide them for resenting our authority—is strong But they are not children they have a lifetime of experience and responsibility behind them which they do not forget, and many of them feel that when plans are made on their behalf they ought at least to be consulted Miss A M SHERIDAN [22] has lately pointed out some of the hardships which high handed methods may cause A sudden decision to discharge an old person from hospital, so as to free his bed for another, may come as a serious psychological shock to him—a shock which may or may not be mitigated when he learns that plans for his future (based on his doctors' prognosis) have already been made If he protests at being sent to a residential home or hostel he is called "difficult," a label which patients of any age do well to avoid Yet his fault may be no more than resistance to what the hospital staff consider best for him, and, as Miss SHERIDAN says, "what they consider best coincides, in a surprisingly large number of cases, with the quickest and easiest way of clearing the bed " Admission to a residential hostel may mean, for him, consenting to give up the home in which he has lived for forty or fifty years and going to a new home among strangers—not a decision (she points out) which anyone would like to take at short notice and without due inquiry Again, he may never have been asked for some simple information which would have influenced those shaping his destiny She mentions the case of a woman transferred from a hospital in the north of England (whither she had been evacuated in 1939) to a region where she was believed to have relatives Not until she was on the train was she told where she was going and why whereupon she explained that she had no relatives whatever in that part of the country

Discharge without due warning may mean hardship not only to patients but also to their families They may have nursed a mentally disturbed or incontinent patient devotedly for many months before a bed could be found for him, and may have suffered great physical fatigue, as well as feelings of fear, disgust, or inadequacy If they are not prepared in advance for for his discharge, fortified by regular accounts of his progress, given time to prepare for him, and helped to solve the problems his return will create, they are apt to panic and say that they cannot have him home They, too, are then called "difficult", and are cited as examples of the way the Welfare State undermines our sense of responsibility for elderly relatives But a sense of responsibility, as Miss SHERIDAN remarks, is a thing of slow growth, planted by early training and developed by experience in the middle-aged children of our elderly patients it came to maturity long before the Welfare State was born Those who seek to evade reasonable responsibility, she says, are the same people as would have done so before the days of the National Health Service Most relatives, provided they are properly prepared for it, are cooperative about having elderly patients back again

In these matters, the task of the almoner is to give help alike to patients, relatives, and hospital staff She must resist any temptation to take the responsibility off the family by "organising" some thing instead she must give them the sort of help which enables them to solve their problems for themselves To do this she must see the patient and his family early in his treatment ("long before he has become a 'social problem' in the eyes of the medical and nursing staff"), and with experience she soon comes to know the combination of prognostic and domestic circumstances which are likely to produce trouble later She can thus anticipate and mitigate the difficulties which may come from unexpected and sudden notice of discharge, arrange assistance well in advance for those who will need it, and recognise early the cases in which discharge home will prove impossible She may then have to tell the doctors that a patient they wish to discharge still requires more nursing and care than can be arranged for in the average household, and she may have to explain, not once but many times—especially to junior medical staff, who come and go—that domiciliary services and residential homes and hostels all have their limits She may have to tell doctors—and sometimes, Miss SHERIDAN finds, she tells them in vain—that no satisfactory arrangements can be made for a patient they propose to send out

It is part of the almoner's accepted duty to do these things yet surely it should not be hers alone. Surely the doctor who discharges a patient should have a full and clear idea of what is to become of the person on whom he has spent much time and skill, and should himself be satisfied with the proposed arrangement ? His concern for those on the waiting list is bound to exceed his concern for those for whom he has already done his best, but it should not outweigh it entirely He should share with patient, almoner, and relatives the duty of seeing that the good work of the hospital is not wasted

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[22] [illegible] 7, 411

## Man in Space

SPACE flight is already with us Space travel (not to be confused with interplanetary travel) will come before long [1], but the needs and reactions of man in space must be determined before the aeronautical engineer can begin his drawings Unmanned balloons have reached an altitude of 40 miles, and rockets of about 250 miles, but so far the highest that man has reached is 72,395 feet (about 14 miles) in a balloon ascent by STEVENS and ANDERSON in 1935

For space travel a completely self contained sealed cabin is essential This will have to pass rapidly through the air, where, although the temperature falls with increase of altitude, friction and compression cause great heat, then through a region of high temperature containing toxic amounts of ozone, then through a region of great cold, and finally into space, where solar and other radiations maintain the temperature at about 4000°F Accordingly the crew will have to be protected against both overheating and overcooling and for this purpose it may prove possible to devise a system of reflectors and absorbers to maintain the temperature within the comfort range of 60–75°F The other main problems are removal of carbon dioxide and other excreta, the supply of oxygen, pressure radiation, weightlessness and acceleration and deceleration. A carbon dioxide concentration of 6–7% becomes distinctly uncomfortable after a time, especially at low oxygen tension, and more than this is dangerous Carbon dioxide and water vapour could be removed from the cabin by chemical absorbers, but these are bulky and their margin of safety is small. It may be possible to arrange that, after absorption, the gas is released and passed through air locks into space thus freeing the chemical for repeated use Similar methods will have to be developed for other excreta, such as methane, amines volatile oils, and the products of bacterial fermentation of fæces and urine Normally these substances never reach a toxic concentration, but in a confined cabin some might do so, in addition, many are disagreeably odorous The oxygen-supply can probably best be carried as a liquid in fibre glass or other containers from which it must be delivered with the least possible waste. In high altitude flying (which is quite different from space travel) compressors can be used to force the outer air into the cabin at the necessary pressure but in space, where there is no outer air the pressure-developing mechanism must be incorporated in the outfit for supplying oxygen. Probably crews will have to be acclimatised to high altitude in order to keep the internal cabin pressure as low as possible and so reduce the strain on the hull whose outer side will be in a virtual vacuum When breathing air man can live and work at 16,000–18,000 feet breathing pure oxygen he can operate at an equivalent of 45,000 feet (a pressure of 110·0 mm Hg), but in practice the equivalent of a somewhat lower altitude would be safer Fortunately, pure oxygen appears to be non toxic at altitudes above 15 000 feet Ultraviolet light would probably not be a hazard inside the cabin, but some of the heavy primaries of cosmic radiation might pierce the hull and cause delayed effects No doubt, non penetrable materials will be found for the hull In space man and materials would have mass but no weight, owing to the absence of gravity forces The resulting loss of elastic deformations would probably not impair most physiological functions The main difficulty would be the altered stimuli from the vestibular and anti gravity systems Normally there is a base-line of stress from which we judge position at rest and in movement, and without this base-line an entirely new coördination would have to be learnt unless the cabin were supplied with a rotational device to simulate gravity Further, where there is no gravity there is no convection, so a highly efficient air stirring system must be provided, to prevent the crew suffocating in its own expired air At present rocket craft move in space in a bizarre and far from smooth manner that would cause prostrating motion sickness this is a problem for the engineers Visual adaptation will be necessary In gasless space there is no light scatter, light is brilliant, shadow totally dark and the visibility range almost limitless So much for space itself but it has to be reached and left This means that the crew must undergo enormous acceleration and deceleration. During the development of high-speed aircraft much has been learnt of how to lessen the harmful effects of such changes, but more needs to be known

If man with the help of machines can adapt himself to space it will be as great a step as from water to dry land. We may surely imagine that the step will be taken. After all did any silurian JULES VERNE dream that even his remotest cousin would one day breathe air ! Yet that is what we do

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[1] Those interested may consult (a) Physics and Medicine of the Upper Atmosphere Edited by C. S. WHITE and O. O. BENSON Albuquerque: University of New Mexico Press, 1952 (b) Man's Milieu in Space By R. M. FENNO J. Aviat. Med. 1954, 25 612. (c) Aviation Medicine in its Preventive Aspects. By J. F. FULTON. London: 1948

## Annotations

### RESUSCITATION OF THE NEWBORN

Two years ago Donald and Lord [1] stated 'Every year in England and Wales about 14 000 children die in the first month of life, and of these about 2300 are certified as dying of asphyxia and atelectasis ' In an attempt to break what they called the vicious circle of anoxia, œdema, and atelectasis ' in newborn infants in respiratory distress Donald and Lord introduced a servo patient-cycled respirator, ' which aids inspiratory efforts in phase with natural respiratory movements without the imposition of regular periodic pressure changes which are often opposed to the patient's own spontaneous efforts

Parallel with efforts along these lines to improve the oxygen supply and keep the airways open several workers in the United States had turned their attention to the possible use of detergents to expand collapsed lungs on the ground that such agents would encourage formation of air liquid interfaces at points where the respiratory surfaces were apposed thereby improving aeration of the whole lung Gruenwald [2] in 1947 claimed that a surface active substance, amyl acetate, reduced the pressure necessary for expansion of infants lungs post mortem and he suggested that the addition of such a substance to the inspired gas might relieve the initial atelectasis of the newborn In 1952 this began to seem feasible after the introduction into clinical work of a non ionic detergent of remarkably low toxicity ( Triton A 20 ' latterly called Triton WR 1339 ) which had been used in the strepto mycin-aerosol treatment of pulmonary tuberculosis,[3] and to ease the expectoration of viscid mucus From experiments on himself and on rats, Miller concluded that this detergent (an alkylaryl poly-ether alcohol) could safely be administered in effective concentration by aerosol. Ravenel[4] reported the successful treatment of 18 infants with massive atelectasis or aspirated fluid, whom he exposed to a nebulised mist of ' Alevaire ' (5% glycerine, 2% sodium bicarbonate, and 0 5% triton WR 1339 in distilled water) In his view the use of alevaire would save a substantial proportion of patients with neonatal atelectasis Bloxsom[5] has made a further study with alevaire, using it both as a primary agent and to hold the spreading factor, hyaluronidase, in aerosol suspension He claims that in neonatal atelectasis lung expansion proceeds more rapidly when spreading factor and detergent are combined The argument for incorporating hyaluronidase seems somewhat tenuous , but in the five cases reported by Bloxsom this combination was apparently successful where oxygen therapy alone was not

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[1] Donald I Lord J *Lancet* 1953 i 9
[2] Gruenwald P *Amer J Obstet Gynec.* 1947 53 996

The efficacy of detergent treatment of atelectasis cannot yet be evaluated , but the early results are promising, and this type of adjuvant therapy certainly deserves attention

## POST TRAUMATIC PAINFUL STATES

INJURY is normally followed by an orderly progression of repair together with disappearance of pain, œdema, and any associated vasomotor changes This sequence is complex and ill understood, but it is usually so rapid and certain that we are surprised and even indignant when the pattern is changed That major and minor trauma may be followed by persistent pain, vasomotor disturbances, osteoporosis, soft tissue atrophy, and gross loss of function, has long been recognised Mitchell[6] gave an excellent clinical description of causalgia from the many cases of peripheral nerve injury which he studied in the American Civil War, and thirty years later his son found that in some the pain had continued unabated The intense burning pain, which most commonly follows damage to the median and sciatic nerves, is characteristically enhanced by any circumstances which initiate sympathetic activity , and Doupe et al[7] suggested that the injury causes a failure of fibre insulation, allowing the vasoconstrictor impulses to short circuit to the afferent pain fibres Causalgia is greatly relieved by sympathectomy

There are many painful states which follow minor nerve and soft tissue trauma that are less well defined Various descriptive titles have been applied to these, often according to the dominant symptom or to the observer's impression of their pathogenesis , minor causalgia, reflex dystrophy, post-traumatic dystrophy, and traumatic neuralgia are some of the many The degree of trauma is unrelated to the severity of the symptoms, and rarely the trauma may be trivial without breach of the skin surface Most commonly perhaps, the post traumatic painful state follows division of a small peripheral nerve The pain may be spontaneous or be aroused only by cooling or touch It may be burning or aching , and on this major pain may be superimposed unpleasant bizarre sensations, such as tingling or a feeling of electric shock The threshold for pain both in the skin and the deep tissues is much lowered, and the patient alertly guards the extremity from any mechanical contact Œdema and vasodilation occasionally develop in the early stages , but the skin is usually cold, cyanosed, thinned, and covered with perspiration The connective tissue, joint capsule, and bone show varying degrees of atrophy

Casten and Betcher[8] have reviewed their therapeutic experience with this chronic disorder, which they term reflex sympathetic dystrophy The patient is told about the nature of the disorder and reassured about the eventual outcome, and his cooperation is obtained Function is improved by physiotherapy, and the sympathetic pathway to the limb is interrupted by procaine ganglionic blocks or by ganglionectomy Ganglionic block, they suggest, is best achieved by continuous paravertebral infiltration of local anæsthetic for up to three weeks Of 147 cases 82 showed an excellent response, 56 were improved, and only 9 did not respond The value of interrupting the sympathetic pathway in post traumatic painful states has been described previously (many believe that it benefits the patient by improving the peripheral circulation rather than by relieving pain) Paravertebral infiltration of local anæsthetic is such a simple measure that it should always be tried in these distressing cases

## MYOPATHY AND MYOSITIS

MYOPATHY, or muscular dystrophy, is usually regarded as a progressive degenerative disorder of voluntary muscle fibres in which regeneration does not occur Improvement, but not recovery, has been claimed after the administration of glycine, of vitamin $B_6$, and of wheat-germ extracts , but controlled studies[9 10] have not supported these claims The rate of deterioration varies greatly , in the disease starting in childhood, in which pseudo hypertrophy of muscle is common, there is usually a relentless downhill course, and commonly the child is bedridden after three or four years When the disease starts in late adolescence or in early adult life, either as the facio scapulo-humoral type of Landouzy and Déjerine or as the shoulder and pelvic girdle type described by Erb, deterioration may be extremely slow, and in some patients there are long periods in which the disease appears to be stationary Professor Nattrass[11] has reported 8 cases in which there was complete or virtually complete recovery Nattrass examined only 1 of these patients during the severe phase of the disease, but clinical records of this stage, when muscular dystrophy had been diagnosed, were available in all 8, and Nattrass examined each of them after their recovery. Of the older reports of apparent recovery, the best authenticated is that by Erb[12] of a boy who at the age of five developed weakness of the pelvic and shoulder girdles and was found by Erb to have the typical clinical characteristics of a myopathy except that the tendon-reflexes were retained By the age of ten this boy had improved considerably, and by the age of sixteen he was well and strong

The cases described by Nattrass appear to fall into two groups 1 or possibly 2 cases were probably examples of the myopathic type of amyotonia congenita—a condition differing in prognosis from classical myopathy The majority of patients who in infancy show the clinical picture of amyotonia congenita have the infantile progressive spinal muscular atrophy described by Werdnig and Hoffmann,[13] but Batten[14] suggested that amyotonia congenita could also be produced by a benign infantile myopathy, and this supposition was later confirmed by a long term follow-up of an affected family and necropsy of one of the family who died of bacterial endocarditis[15 16] The other 6 cases were of a different type These were in 4 boys and 2 girls who developed symptoms of muscular weakness between the ages of three and ght, in all of them the weakness appears to have fected predominantly the proximal limb muscles, in at pseudo-hypertrophy of some muscles was present, d in all the weakness seems to have become rapidly rse In each of these 6 muscular dystrophy was gnosed, but they all recovered from their muscle eakness after two to seven years One case is of especial terest, since a male cousin had died at the age of fifteen th supposed progressive muscular dystrophy but fortunately clinical records of this cousin s illness were t obtainable. In the other 5 there was no known mily *history of neurological disease* There was a mous feature in the patient with the positive family story in that he had two separate attacks of muscular eakness and in the second attack severe muscle wasting recovered completely from each of the attacks As gards treatment 1 patient received *nicotinic acid and* injections of chorionic gonadotrophin, but in neither d improvement seem to be related to the administration these substances, 3 other patients were given wheat erm, and in all 3 improvement started shortly after the tart of this treatment

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[3] Miller, J B Boyer E H J *Pediat* 1952 40 767
[4] Ravenel S F J *Amer med Ass* 1953 151 707
[5] Bloxsom A *Anesthesiology* 1955 16 41
[6] Mitchell S W *Amer J med Sci* 1878 76 17
[7] Doupe J Cullen C R Chance G Q J *Neurol Psychiat* 1944 7 33
[8] Casten D F Betcher A M *Surg Gynec Obstet* 1955 100, 97
[9] Fitzgerald, G , McArdle, B *Brain* 1941 64 19
[10] Walton, J N , Nattrass F J *Ibid* 1954, 77, 169
[11] Nattrass F J *Ibid* p 549
[12] Erb W *Münch med Wschr* 1908 55 2121
[13] Brandt S Werdnig Hoffmann's Infantile Progressive Muscular Atrophy Copenhagen 1950
[14] Batten F E *Quart J Med* 1909 3 313
[15] Turner J W Aldren *Brain* 1940 63 163
[16] Turner J W Aldren *Ibid* 1949, 72, 25

In retrospect Nattrass doubts whether the diagnosis muscular dystrophy was correct in any of these 6 atients. He suggests that they in fact had polymyositis, nd points out that in all the cases the onset of muscle eakness was more rapid than in typical muscular ystrophy In 1 of the patients there was a history of ransient dysphagia, a feeling of stiffness of the muscles nd mild Raynaud s phenomena (a sister also had attacks f coldness and pallor of the fingers) which might support he diagnosis of polymyositis but the other cases would eem to be fairly typical examples of muscular dystrophy xcept for the rapid onset and their recovery

The classification and ætiology of myositis are still disputed. In addition to bacterial infections such as the rare suppurative myositis and gas gangrene and the parasitic infestations, such as trichinosis and toxoplasmosis, there is the *condition variously known as dermato*myositis or polymyositis according to the degree of skin involvement The ætiology of this condition is unknown but it does not seem to be due to an infection The essential pathological feature is acute hyaline necrosis of muscle fibres[17] *with interstitial cellular infiltration in* the affected muscles In the cases with relatively acute onset there may be skin eruptions but in the slowly developing cases skin lesions are usually absent The patients complain of considerable weakness and fatigability of the affected *muscles and in the later stages* wasting and fibrous contractures are found Commonly the muscles of deglutition, and sometimes the respiratory muscles, are involved Some of these cases have a progressive downhill course but others particularly those with an acute onset, may *become stationary and eventu*ally recover Polymyositis is rare and the diagnosis is easily overlooked since it may mimic better known disorders such as polyneuritis myasthenia gravis[18] and muscular dystrophy Nattrass urges the importance of muscle biopsy in cases of apparent muscular disease This is certainly valuable in many cases but the interpretation of muscle lesions especially in biopsy specimens, may be difficult This difficulty is illustrated by the contrast between his statement that the pathological changes in polymyositis are very different from those of muscular dystrophy with that of Adams Denny Brown, and Pearson[17] who say that there is no essential difference between the most chronic changes seen in some muscle fibres in chronic forms of polymyositis and the changes that are seen in the more rapid forms of muscular dystrophy

We cannot be sure whether these 6 cases reported by Nattrass and the few described previously were in fact polymyositis or muscular dystrophy which for some reason cleared up But Nattrass s paper indicates the importance of further study of these rather neglected disorders of muscle, and also the need for careful thought *before giving the usual gloomy prognosis* in cases of apparent muscular dystrophy starting in childhood

## PALMAR BLOOD-SUPPLY

MOST incisions in the hand heal well, provided they are planned to follow the lines of the skin flexion-creases But necrosis of the palm occasionally follows the widespread undermining of skin which may be necessary in the radical treatment of Dupuytren s contracture Conway and Stark[1] by injections of the hand in the cadaver, have brought to light two important anatomical facts Firstly, in the centre of the palm the vessels are scanty, and *thus area is relatively ischæmic* whereas in the thenar and hypothenar eminences and in the fingers the vessels are more densely arranged The areas of relatively great density correspond in general to areas in which arteriovenous anastomoses are found[2] Secondly, the arterioles of the palm pass perpendicularly from the deeper vessels to the skin surface From this study it is clear that extensive undermining in the palm may sever vessels passing to an area which is never well supplied with blood; and thus a second incision may be less damaging in the treatment of extensive contractures. When there is any doubt about the viability of the skin flaps a full thickness skin graft may produce more rapid healing and a sounder palm

## DIVERTICULITIS OF THE COLON

IN the past treatment of diverticulitis was defensive Until a complication arose this disorder was regarded as a medical problem, if obstruction fistula, or other complications supervened, colostomy was all that surgery offered A more offensive note was struck by Welch et al[3] who suggested that uncomplicated diverticulitis must now be accepted as an important indication for operation They reasoned that patients should be relieved of the unpleasantness of exacerbations, which tend to recur, that the longer symptoms persist the greater is the chance of complications and that the earlier the operation the better is the opportunity for resection and the easier is it to do 582 patients with this condition were seen by them at the Massachusetts General Hospital between 1942 and 1953 114 required resection and only 3 died whereas among 13 patients in whom only colostomy or cæcostomy was done there were 4 deaths associated with operation In a third of their cases it was possible to resect the area at *one operation but temporary colostomy was needed in the* majority Lloyd Davies[4] also believes that it is advisable to intervene and resect before worse befalls the patient. Experience at St Bartholomew s Hospital between 1923 and 1932 when no resection was done supports this view, for of 34 cases admitted 15 died from complications and 14 had permanent colostomies.[5]

The decision to operate on the uncomplicated case is not always easy but there should be no hesitation in patients under 50 in those who have had repeated attacks, or in those with urinary symptoms which presage the development of a colovesical fistula Finally there are occasions when it is well nigh impossible to exclude the possibility of carcinoma Colock and Sass[6] have compared 50 patients having diverticulitis with a similar number suffering from carcinoma The difference between these two groups was not so much in the character of the symptoms and signs as in their frequency, which confirms the difficulty of differentiation in individual cases Where doubt remains resection is obligatory

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[18] Matthews W B, Burne J C J *Neurol Psychiat* 1953 16 49

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[2] Wood Jones F The Principles of Anatomy as seen in the Hand London 1944
[3] Welch C E Allen, A W Donaldson, G A *Ann Surg* 1953 138, 332
[4] Lloyd Davies O V *Proc R Soc Med* 1953 46 407
[5] Todd, I P *Ann R Coll. Surg Engl* 1955 16, 118
[6] Colock B P Sass R I *Surg Gynec Obstet* 1954, 99 627

## INACCURACY IN THE LABORATORY

Two years ago we referred to evidence that different biochemical laboratories might report very different results of analysis of the same sample[1] Since then the International Association of Clinical Biochemists has made a survey, mainly in America and the countries of Western Europe, and we understand that the findings (not yet published) show that the situation is much the same in all the countries studied

We suggested that it would be useful if someone supplied accurately analysed blood plasma or serum so that individuals could check their own analyses Glaxo Laboratories Ltd are now preparing batches of freeze-dried serum, and this material is being analysed by members of a joint committee set up by the Association of Clinical Pathologists and the Association of Clinical Biochemists It is proposed to supply figures for the content of sodium, potassium, calcium chloride, urea, glucose, and total protein The samples are to be distributed by Messrs C Davis Keeler Ltd, 39, Wigmore Street, London, W 1, to whom all inquiries should be addressed Large scale production, and the good will of the firms concerned, have enabled the costs to be kept low, and it is expected that each sample will cost less than five shillings

## ELECTROPHORESIS OF SERUM-PROTEINS

In 1937 Tiselius[2] separated the components of the plasma-proteins by boundary-electrophoretic analysis, and analysis by this method of normal[3–7] and pathological[4–10] sera has since been often recorded The apparatus needed for boundary electrophoresis is complex and expensive, and its use entails much time and technical skill But the development of zone electrophoresis on filter-paper, with apparatus which is simple and cheap, has now brought the electrophoretic method of protein separation within the reach of most hospital laboratories

McQueen et al[11] have reviewed the results of paper-electrophoresis of serum-proteins in several different diseases They conclude that the protein pattern is specific in collagen diseases, nephrosis, hepatic cirrhosis, and multiple myelomatosis They have also found that serial observations are of great value in assessing the progress and activity of a disease, especially in collagen diseases and infective hepatitis McQueen et al suggest that paper electrophoresis of the serum proteins may replace the turbidity and flocculation tests for diagnosis and serial assessment of infective hepatitis This enthusiasm is not shared by Church and Blackburn,[12] who found that electrophoresis of serum-proteins in cases of liver disease gave no more information than could have been obtained more simply from zinc sulphate turbidity tests and estimations of total serum-proteins Mackay and Volwiler[13] point out that the usefulness of paper-strip electrophoresis in routine diagnostic work is limited *by the fact that changes in the serum-protein fractions* are generally non specific to any particular disease Exceptions to this are γ-myelomatosis and agammaglobulinæmia, where the method may give results of diagnostic value Mackay and Volwiler conclude that "quantitative reproducibility of paper electrophoretic analysis of serum appears satisfactory," but they do not claim the same precision as for boundary electrophoresis The quantitative accuracy of paper electrophoresis has been questioned by Martin and Franglen,[14] who also point out that the technique must be very careful if useful and reproducible qualitative results are to be obtained It seems that the application of this method to clinical work would best be confined to qualitative assessment of the stained strip by someone experienced in such work The results of quantitative analysis are often inaccurate and may be misleading

## INFUSIONS INTO BONE-MARROW

As long ago as 1922 Drinker et al[15] and Doan,[16] working independently, showed that fluids infused into bone marrow quickly reached the general circulation Josefson[17] gave patients with pernicious anæmia liver extract by the medullary route, he noted transient reactions, but proposed that other drugs should be given by this route But it was Tocantins et al[18–22] who first made extensive use of intramedullary infusions of blood, saline, and dextrose solutions for replacement therapy This method has been used for massive infusions in a case of ulcerative colitis, the patient received nearly 23 litres of blood and saline and dextrose solution into his sternal bone-marrow in nine days[23] Until quite lately intramedullary infusions were given into the sternum or, less commonly, into the tibia[24] or femur[25], and special instruments have been designed for penetrating the bone and delivering the infused fluid[24 26] Pillar[27] has shown by injection of radio opaque material into the iliac marrow that the injected material rapidly reaches the general circulation, thus confirming earlier observations[18 21] He found that the crest of the ilium was a good site for infusion, because the capillary network inside the marrow is here more extensive than that in the sternum and most other bones, and because accidental perforation of the ilium does not endanger vital organs He infused solutions of the vitamin B complex, vitamin C, dextrose, and potassium chloride without ill effect

Bone-marrow infusion is contra-indicated in cases of bacteræmia or septicæmia or even of extensive sepsis, as in generalised peritonitis, because of a real danger of causing osteomyelitis[28 29] Mediastinitis[30 31] and perforation of the posterior table[26] have followed infusion into the sternum There is some experimental evidence that infusion into marrow may cause fat-embolism,[32] but this complication has not been reported in man Medullary infusion is unsuitable for continuous replacement or maintenance therapy over any length of time Viscous fluids, such as blood, must be infused under pressure, so such an infusion needs constant attention Nevertheless anyone with experience of protracted parenteral maintenance therapy must at some time have wondered whether a patient would die from lack of veins capable of receiving infusions, and it is in this type of case, and in those where veins are collapsed, that intra osseous infusion is of greatest value

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[3] Dole V P *J clin Invest* 1944 23, 708
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## Special Articles

# THE ACTION OF CHLORPROMAZINE

## REVIEW OF FRENCH WORK

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THE synthesis of chlorpromazine was the culmination f twenty years' research directed towards the discovery f a drug which would either prevent or modify the effects which follow irritation (as opposed to either simple section r stimulation) of sympathetic nerves (Decourt 1954 Reilly and Tournier 1954) These effects are known in rance as the phenomena of Reilly and the syndrome of rritation Reilly et al (1934) described the condition rst as 'hæmorrhages, vascular and lymphatic lesions f the alimentary tract, produced by perisplanchnic njections of different substances' including very small oses of bacterial toxins, chemical irritants and physical gents—e.g., trauma and electrical stimulation Although he organs affected varied with the nerve irritated the macroscopic and microscopic lesions did not vary and were non-specific Hæmorrhage and necrosis of the suprarenal glands were a constant finding The condition was rapidly fatal, the animals dying within a few hours n a state of cardiovascular collapse indistinguishable rom irreversible shock. Animals which survived for a ew days showed an accumulation of fat in the liver ; his, however could be prevented by section of the spinal ord at D7 and by denervation of the liver Less intense rritation produced sclerosis and endarteritis Renal fibrosis and hepatic cirrhosis have been reported

### Phenomena of Irritation

A feature of the syndrome is that the lesions are widespread and often far removed from the original site of irritation Thus, violent irritation of the splanchnic nerve, besides causing visceral lesions, can induce intense cerebral congestion perivascular and pericellular œdema, and even hæmorrhages.

Reilly and Tournier (1954) admit that, if the phenomena of irritation only appear after contact of the noxious agent with autonomic nerves one might argue that an arbitrary experiment has little resemblance to the conditions in acute infections and toxæmias. These workers however have produced both the visceral and cerebral lesions by injecting irritants into any mucosa rich in autonomic nerve fibres particularly the pharyngeal mucosa.

The widely different pathological lesions which can follow an acute infection of the pharynx and neighbouring structures are well known and in this instance there is a close parallel between the experimental findings and clinical experience

Reilly's work was confirmed by other workers in France (Hatinel and Conte 1936 Pham 1935)

Tardieu (1942) produced typical visceral lesions by irritating the cerebral peduncles and by injecting an infinitesimally small dose of typhoid antigen into the third ventricle of a dog; this immediately induced a typical typhoid state

The necropsy findings in patients dying from acute fulminating infectious states were shown by Marquezy et al. (1935) to be the same as those produced experimentally by irritating the nerves. They concluded that these states were the result of the action of the bacterial toxins on autonomic nerves and not on the capillaries or the cells of the organs affected, as is generally believed

### *Relation to Reaction of Alarm*

Decourt (1951) has compared lesions described by Selye as following the reaction of alarm with the phenomena of Reilly The macroscopic and microscopic appearances of both the acute and the chronic lesions are very much alike Reilly, however produces the effects by placing irritants in direct contact with, or in close proximity to autonomic nerves in amounts which would be innocuous by injection elsewhere Selye, on the other hand, applies in an arbitrary and widespread fashion more powerful irritants, which have therefore only an indirect effect on the autonomic nervous system.

### *Ætiology*

There is a strong difference of opinion about the cause of the lesions Selye (1952) attributes only a minor rôle to autonomic disturbance but does not explain how the vital pituitary adrenal responses are brought into action

Reilly attaches little importance to endocrine response to irritation but admits it may play a part He appears convinced that reflex autonomic nervous activity is the cause of his phenomena He cites experiments by Tardieu et al (1954) which show the existence of pathogenic impulses passing from the brain to the periphery during the evolution of the phenomena of Reilly These impulses are believed to pass through the sympathetic nerves

### Attempts to Prevent Phenomena of Irritation

It appeared logical to search for a drug which would prevent reflex sympathetic activity which appeared to be directly connected with the phenomena. Since 1935 extensive but unsuccessful trials have been made with antagonists of adrenaline ganglion blocking drugs, pituitary extracts, procaine, and atropine alone and in combination and in a very high dosage (Tardieu et al 1954)

Tinel et al (1935) suggested that the phenomena were caused by histamine released by an axon reflex Synthesis and trial of many anti histamine drugs showed that these were quite ineffective (Decourt 1954) Clinicians however claimed that phenothiazine derivatives, especially promethazine and diethazine, in association with general anæsthesia reduced both surgical shock and the amount of anæsthetic agents required (Laborit 1950) Similar claims were made for ganglion blocking drugs and even for curare (Romani 1952, Laborit 1948)

### *Chlorpromazine*

It was not until chlorpromazine (a phenothiazine resembling promethazine) became available that any significant progress was made in preventing the effects of both peripheral and central irritation With this drug Reilly et al. (1953) and Reilly and Tournier (1954) protected 70% of guineapigs against splanchnic irritation which was fatal to 90% of controls The dosage was 5 mg per kg of body weight which is admittedly large. These workers showed that the addition of ganglion blocking and anti histamine drugs did not offer any advantage Cooling was useless ; indeed the prevention of hypothermia appeared to hasten recovery

This work only established the protective value of chlorpromazine. Its use in high dosage when a toxic state was established appeared to intensify it and to hasten the end Smaller doses increased gradually prolonged survival but did not decrease mortality

The central action of chlorpromazine was established after intraventricular injection of a dose of 1 mg per kg of body weight produced reversible narcosis and prevented the hypertensive responses which normally follow stimulation of the central end of the cut vagus nerve (Cathala and Pocidalo 1952)

With chlorpromazine Tardieu et al (1954) and Pocidalo and Tardieu (1954) prevented the effects of irritation of the cerebral peduncles caused by injecting necrosing solutions. Normally the animals died within a few hours, showing typical pulmonary and intestinal hæmorrhagic lesions with vasomotor collapse. Preventive administration of chlor promazine by intravenous infusion either attenuated or inhibited these effects

It is significant that all the successful work in preventing the phenomena of Reilly was achieved by using chlorpromazine alone The temperature-reducing properties of chlorpromazine were not considered important No curative properties were claimed for chlorpromazine, and its action appeared essentially preventive

### *Mode of Action*

It is now generally acknowledged that chlorpromazine does not possess ganglion-blocking properties resembling those of the methonium compounds (Decourt et al 1953b, Huidobro 1954) Courvoisier et al (1953) originally suggested this properly because they observed an antagonism to acetylcholine, and prevention of the effects of stimulation of the peripheral end of the cut vagus In a concentration 10 mg per kg of body-weight chlorpromazine depresses the ganglionic cell directly and reduces its activity (Decourt 1954)

Its anti adrenaline properties cannot explain the effectiveness in countering the syndrome of irritation, because in the past equally potent anti adrenaline drugs have not been of any experimental or clinical value (Decourt 1953, Tardieu 1954a and b) Therefore its central action is the property which deserves consideration and may explain its reported value in such a wide variety of clinical states

Terzian (1952) noted that the electro encephalograms of animals under the influence of chlorpromazine closely resembled those of physiological sleep This indicated an activity on the centre of wakefulness situated in the anterior part of the reticular formations of the mid-brain

Angeleri et al (1954) confirmed this action on the reticular formations and noted that there was little or no modification of cortical sensory activity, although activity of the reticular formations was abolished Hiebel et al (1954), who made a detailed study of the action of chlorpromazine describe three ways in which it acts on the reticular formations

(1) Chlorpromazine suppresses the disturbances activated through the reticular formations as the result of sensory or nociceptive stimuli. It shares this property with promethazine and small doses of narcotics—e g , chloralose and barbiturates The greatest effect, however, is obtained in strength of 1 mg per kg of body weight, and increase of dosage never produces either deep anæsthesia or the cortical tracings typical of that state

(2) Chlorpromazine also suppresses the central activating *effects of peripheral sympathetic discharges or of the injection* of a small dose of adrenaline, which Bonvallet et al (1953, 1954) have shown to be caused by a humoral mechanism It is suggested that the peripheral anti adrenaline action of chlorpromazine may be active here

(3) Chlorpromazine has been shown to unmask the inhibition of the reticular formations which follows distension of the carotid sinus This action is usually obscured by the peripheral stimuli which would accompany this distension under normal conditions

After reviewing recent neurophysiological research into the relationship between the cortex and the reticular formations Hiebel et al (1954) recall that the reticular formations are believed to play an important part in conscious and autonomic activity, and that depression of the reticular formations may have far-reaching consequences

(1) Chlorpromazine can considerably decrease the state of wakefulness and raise its threshold without causing narcosis

(2) Since the reticular formations control muscle tone, their depression will be followed by a decrease in muscle tone, as observed by Burn (1954)

(3) The reticular formations control body temperature, vomiting, and sympathetic tone, and an over all depression in their activities can be expected from chlorpromazine

(4) [illegible] tion of the anterior lobe of the pituitary gla[illegible]ession has been linked with a central action of adrenaline in the region of the corpora mammillaria and the posterior part of the hypothalamus, which in particular control the secretion of corticotrophin Hiebel et al (1954) suggest that there is no doubt that chlorpromazine could depress the activity of adrenaline in this part of the brain

This last suggestion has been investigated by several workers, and in animals the suppression by chlorpromazine of pituitary-adrenal response to stress has been shown by Aron et al (1953) and Castaigne (1954) after Benos (1951) had shown that promethazine depressed the response

Castaigne (1954) bases his report on experience of the action of chlorpromazine on more than 2000 rats, in which he induced general anæsthesia more than 4000 times He is careful not to draw conclusions about man from this work, for the doses used exceed the clinical dosage His findings are, however, of great importance in that they point the way to future research into the action of chlorpromazine in man, especially in association *with general anæsthesia*

Castaigne has shown in the rat that the addition of chlorpromazine (50 mg per kg ) to an anæsthetic agent completely suppresses the pituitary adrenal response to aggression or stress This medicinal hypophysectomy is transitory and does not affect the subsequent reactivity of the pituitary gland The suprarenal glands still react to the injection of corticotrophin while the rat is under the action of chlorpromazine

" Lytic cocktails " do not give such clear-cut results as does chlorpromazine alone, and full hibernation (with cooling) increases mortality Chlorpromazine and anæsthesia, which are not toxic to the healthy rat, become toxic when the rat is cooled Castaigne thinks that chlorpromazine would increase the toxicity of any of the drugs in the lytic cocktail The action is independent of sleep and has been observed in rats which did not sleep The gonadotropic hormones are also suppressed, and probably all the functions of the anterior lobe of the pituitary gland are affected

In large dosage oliguria was observed, which could be rapidly turned into diuresis by injecting whole pituitary extract This does not suggest any direct action on the kidney but indicates depression of the central mechanisms which control diuresis

Holzbauer and Vogt (1954) have been unable to confirm the findings of the French workers This is explained partly by the smaller doses used (15 mg per kg ) and failure to allow sufficient time to elapse, and partly by differences in experimental technique (*Castaigne 1955*)

All the evidence therefore emphasises the importance of the central action of chlorpromazine Both Hiebel et al and Castaigne refer to the work of Decourt, who has shown that chlorpromazine is the most powerful of many substances which depress cellular activity in a particular fashion, which he calls narcobiosis

It appears from the experimental work just described that both chlorpromazine and promethazine possess similar central actions, although peripherally one opposes histamine and the other adrenaline

This common central action was observed by Decourt (1953) who recalled that Hess (1925), Sivadjian (1934), and Bovet (1935) had described a similar central action for both natural and synthetic drugs which oppose the peripheral action of adrenaline These actions were as follows

(1) A purely hypnotic action

(2) Intensification (or potentialisation) of the action of *hypnotics and analgesics*

(3) A central anti-emetic action

(4) A central hypothermic action

(5) A central antidiuretic action

(6) Inhibition of conditioned reflexes

(7) Intensification of local anæsthetic action

Decourt (1953) classes all drugs which show this ommon central action in one group irrespective of their eripheral action, which may neutralise either acetyl holine histamine or adrenaline on muscle or glandular ells Since these cells are non nervous in origin, he ontends that this shows a universal depressant action n all cellular life He and his colleagues demonstrated reversible depression of cellular activity in various nicellular organisms possessing no nervous systems—e g acteria, microscopic fungi, infusoria, and sea urchins ggs—(Decourt and Anguera 1953 Decourt et al. 1953a nd c) Furthermore a direct relationship was estab ished, through fishes between the active concentrations or unicellular organisms and those active for higher nimals. Fishes were equally affected whether placed n a medium containing the drugs in concentrations ctive on lower organisms or on receiving an injection n a dosage active on higher animals (Decourt et al 1954)

Chlorpromazine and promethazine showed the highest activity of the many drugs tested their minimal active concentration being 1 in 400 000 and 1 in 200 000 respectively far in excess of the other drugs. The fact that anaerobic bacteria were susceptible to this action suggests that there is no direct interference with oxidative processes. Coliform bacilli appeared resistant and it is suggested that their high content of diastases may explain this resistance and provide a clue to the physiochemical action of these drugs

The presence of a quaternary amine reduces this depressant activity The substitution of a quaternary amine for the tertiary amine present in promethazine to form 'Multergan' (thiazinamium) reduces the minimal active depressant concentration from 1 in 200 000 to 1 in 1000—a two hundred fold reduction in activity (Decourt 1953)

Decourt points out that the histological structure of the reticular formations renders them particularly susceptible to narcobiotic action The reticular formations are made up of numerous nerve-cells with short axons and multiple dendrites which intercommunicate freely An impulse passing through this part of the brain will pass through many cells before leaving as an effector impulse If each cell is depressed, its ability both to receive and to transmit impulses will be reduced. The impulse on passing through a series of cells, will rapidly become attenuated and its strength fall to subliminal intensity before it reaches its objective

On the other hand cortical motor and sensory cells are characterised by long axons and few dendrites Impulses pass through relatively few cells hence in such cells a cumulative depressive effect of chlorpromazine is not observed

This concept is in line with current neurophysiological work, for physiologists recognise the polysynaptic nature of the reticular formations (Moruzzi 1951)

### Summary and Conclusions

The synthesis of chlorpromazine was the culmination of twenty years continuous research in France aimed at discovering a drug which would prevent the lesions which follow irritation of sympathetic nerves.

These lesions resemble closely those described by Selye which follow acute non specific aggression and are produced by the pituitary adrenal response to this aggression

Experiments have been described which show that chlorpromazine alone can prevent the effects of sympathetic irritation and the responses of the pituitary adrenal mechanism to non specific aggression

It is suggested that these results are obtained through a highly developed central depressant action on the reticular formations of the brain combined with powerful peripheral antagonism to adrenaline

The reticular formations are believed to contain centres which control vomiting heat regulation, wakefulness, vasomotor tone, muscle tone and secretion of the anterior lobe of the pituitary gland A general depression of this region will have far reaching effects and explains the diversity of action claimed for chlorpromazine

Chlorpromazine in high dilution has a reversible depressant action on all forms of cellular life It does not appear to affect oxidative processes directly, because anaerobic organisms are susceptible to this action

In clinical dosage (up to 1 mg per kg of body weight) it probably depresses individual cells in proportion to their activity In this way nervous cells would be more affected. The action of chlorpromazine is predominantly exerted on the reticular formations because the polysynaptic structure of this part of the brain facilitates a cumulative depressant effect on the passage of impulses through a large number of depressed cells.

Though chlorpromazine does not exert any direct action on cells of vital organs possibly such cells that are already poisoned by endogenous or exogenous toxins might be still further depressed, with an intensification of toxic symptoms

The central action of small doses of chlorpromazine closely resembles that of general anæsthetics, but larger doses do not produce anæsthesia

The value of chlorpromazine in clinical medicine depends on how far the phenomena of Reilly and the theories of Selye are accepted If the reactions they describe play a major part in all infections and trauma chlorpromazine and allied drugs are worthy of careful investigation and consideration There is already a widespread impression in France and in this country that chlorpromazine and promethazine reduce surgical shock and postoperative morbidity and fatigue The experimental findings offer an explanation and the extent to which this impression is true can only be decided after further clinical study

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# SOME NEW HORIZONS

## Meeting of the National League of Hospital Friends

Two years ago Mr Iain Macleod,[1] the Minister of Health, urged the Friends of Hospitals to concentrate first on the plight of the mentally ill and the chronic sick , and they have been doing so At this year's annual meeting, held in London on March 9, with Mr J P **Wetenhall**, chairman of the league, presiding, a large gathering heard of fresh directions in which they might extend their services

### THE AGED IN THEIR HOMES

Dr E B **Brooke**, physician-superintendent of the St Helier Hospital, Carshalton, spoke with warm gratitude of the work done by friends of hospitals, but added that there is still a vast amount of virgin soil for them to till The aged sick in their own homes are particularly in need of help , for though it is true that "home—other things being equal—is the best place for everybody," yet for neglected old people it can be the scene of tragedy, and sometimes the tragedy happens while they are waiting for a hospital bed He suggested that friends of hospitals might take on not only old people in the wards but old people on the waiting-lists Some of these, faced with long invalidism, are alone and friendless , others are looked after with great devotion by relatives, who may themselves be old and ill Hospitals are now beginning to establish geriatric units, and some send out a geriatric team to visit the home before the patient is admitted to hospital, and assess both the urgency of his case and his immediate needs Hospital friends could be the link between him and hospital while he is waiting for a bed, help him on his return home, and provide him (from a special fund) with the amenities and gadgets he requires He could thus rely on the continued friendship of the same friends, to whom he and his relatives could turn if at any time the responsibility became too great for them Geriatric units are multiplying there are about 60 in the country now Dr Brooke suggested that the league might start forming "Friends of Geriatric Units" Some of the members, he thought, might serve a short apprenticeship with the almoner and social worker, and these could teach old people diversional therapy in their own homes Others might collect funds for equipment—books, magazines, wireless sets, material for occupational therapy, gadgets to help the handicapped, clothes, and so forth Others might maintain a flying squad of helpers willing to tide old people over crises in their homes until a hospital bed became available He quoted some moving cases a woman of 70 with cataract of one eye and incipient cataract of the other, looking after a husband of 93 with senile dementia and a brother of 82 with pneumonia , a man of 79 living alone, washed and fed by a neighbour of 84 , a woman of 84 living in a damp isolated bungalow and writing to beg that a bed might be found for her old demented husband before the weather became too cold for him, and she too tired to carry on Many old people are occupying hospital beds who no longer need full hospital care , and their beds are badly needed by others Many could be discharged if we had more half-way houses, and more complete domiciliary services—meals, laundry, chiropody, transport to hospital for treatment, and the like The hospital should also arrange (as some now do) to take old people in for short periods to give tired relatives a holiday Meanwhile there are great opportunities for voluntary workers to help, and the leagues of friends, who have brought "a leaven of real hospitality into the hospitals," can carry the same leaven into patient's homes

Dr T P **Rees**, physician-superintendent of Warlingham Park Hospital, said that little voluntary work has as yet been done in mental hospitals Most of them were built in the last century, by the State or by local authorities , and because of the widespread unreasoning fear of mental illness the walls were high and the doors locked to visit them was an ordeal Mental hospitals differ from general hospitals in that most of their patients are up and about They also differ from them, and always will, in this whereas the general hospitals bury their failures, the mental hospitals keep them Since these long stay patients usually live out their full span, they form a large proportion of the resident population, and distract the visitor's attention from the fact that nearly 80% of all patients admitted to mental hospitals are discharged within twelve months Yet the standard of a mental hospital must be judged, he holds, not by what it does for its recoverable cases but by what it does for its helpless and chronic patients Before the Mental Treatment Act, 1930, patients could only be admitted under certificate, but since then more and more have been admitted as voluntary patients and these now form about 70% of all admissions Some hospitals are admitting patients without getting them to sign anything at all—"non statutory" patients Patients entering a general hospital, they say, are not obliged to sign anything, so why should a patient who wants to enter a mental hospital ? A voluntary patient can leave hospital after giving seventy-two hours' notice , a non statutory patient, like a patient in a general hospital, can discharge himself at any time he likes Fences and walls round many mental hospitals are being pulled down The fences taken from one mental hospital were put up again to protect the local park—an interesting comment on behaviour inside and outside the mental hospital Locked doors, too, are steadily becoming fewer Some psychiatrists now believe that locked doors make patients worse , and certainly fewer run away when the doors are open there is no fun in running away through an open door The public are visiting mental hospitals much more freely than they used to do, and many of the hospitals are now holding "open" days All these changes are making it easier to get voluntary help Warlingham Park has had, since 1947, a league of hospital friends who have done good work in arranging outings for patients and befriending those who have no visitors. Advances in the medical treatment of the mentally ill have been striking in the last twenty years , but mental illness is not a purely medical problem it is a social problem, which calls for the cooperation of doctors, nurses, social workers, occupational therapists, friends, relatives, employers, and the patient himself The task of all of them is to teach the patient how to live , and this is not always best done behind locked doors An increasing proportion of patients, Dr Rees believes, should be treated in their own homes But there will always be some who need hospital care, and for these the aim should be to make the hospital as little like a prison as possible, and to let patients, while they are in it, live as normally as possible Some recover in hospital but relapse on discharge "surely this means," Dr Rees said, "that there was something wrong with the treatment we should have taught them how to live at home" The hospital should be a therapeutic community, and there is a job in it for everyone concerned with the patient At Warlingham Park monthly discussion groups are held in each ward, at which patients, doctors, nurses, social workers, and friends of the hospital all meet and talk , and all gain a better insight into the problems of the patient, and help to make his return to hospital less likely Voluntary workers can help patients before they come into hospital, afterwards in their homes, and at patients' social clubs "There is no limit," he told his listeners, "to the work you can do to help us"

Dr **Elizabeth Tylden**, assistant physician to the psychiatric department of Bromley Hospital, described w an outpatients' club—the Stepping Stones Club—s been formed. A team of four (three psychiatrists and psychiatric social worker) found they had to treat the ychiatric outpatients of an area with a steeply rising opulation and no increase in mental hospital beds but romley Hospital has a large and active outpatient occupational therapy department The psychiatric team tried e effect of sending some of their elderly patients there for veral days every week and something striking happened a lonely, depressed introspective, somewhat aranoid woman was put at a table with three blind men ho taught her how to make baskets after a few weeks e was saying I think I've been worrying too much bout myself; can't I do something to help these other eople? ' This kind of thing happened not once but any times. At first little jobs were found for such eople in the hospital then as these ran out a system f good neighbourliness was started in which the Friends f Bromley Hospital (who had existed long before they ecame a league with a name) and the five local branches f the Townswomen's Guild joined in It was found that any lonely old people who had been deteriorating could e kept well in their own homes when they were visited elped, and taken to regular gatherings at the houses of the voluntary workers. Younger patients joined a music nd singing group arranged by one of the hospital riends; and another friend started an art therapy group Several patients wanted a drama group and this has lourished two patients who had given up going outside their own homes at all were persuaded to join and are now leading a normal social life Four voluntary workers started a play group for children attending the child uidance clinic and while this was in progress the mothers attended a discussion group with the doctors and social workers in a neighbouring room The results of these activities have been encouraging Mothers are handling their children better, and some patients have found the self-confidence to start on a course of training or to return to a profession they had given up Finally the voluntary workers held a meeting they wanted to be an organisation and to be properly housed So the Stepping Stones Club was formed in which patients can progress from group to group learning to live with other people and to take their share of social responsibility The Friends of Bromley Hospital have helped not only with service but with generous grants Dr Tylden hopes that possibly with help from King Edward's Hospital Fund for London the time will soon come when the outpatient clinic and the club have their own house, to which patients can come any day and find something going on and someone to help them to join in.

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[1] *Lancet*, 1953 i 191

The message of the three speakers, THE CHAIRMAN said, was 'Go out and work harder' He was supported in this opinion by LORD BEVERIDGE, who had been much moved, by the sense of mission the humour, and the humanity of the speakers. He is always being told, he said, that he is responsible for the Welfare State, and he always takes the opportunity of repudiating it The term "Welfare State suggests that only an official can do good to his neighbours: but what we really want is a 'welfare society"—an enlargement of what the family does for its members The League of Friends of Hospitals he said, is doing this very thing—going out and by personal friendship, personal action, enlarging the family

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## Public Health

# THE NEED FOR OVERLAPPING*

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IN the pursuit of new knowledge opportunity is nowadays almost limited to the specialist Yet never the history of medicine has it been more necessary have a doctor who can look on the individual as a hole What perturbs me—as an administrative medical ficer of health who is trying to see that health amenities nd medical facilities of the highest order are available every person within his community—is to see the on curtains" that are being set up between the ferent specialties in such a way that the individual confined by one or other These barriers are being t up not only between the medical and other social rvices but between the different branches and specialties medicine itself.

When Sir William Beveridge and his committee were ed to prepare a scheme to provide social security for people of this country he made it clear in his famous ort that there were five giants in the road of construction These were named as Want Disease norance Squalor and Idleness He insisted that they med a united obstruction to progress and that they d to be fought singly and together if we were to quer them You will notice that disease is but one these giants; and though by the National Health vice an attempt has been made to organise the resources of medicine to fight this one great giant, nobody intended that this struggle should take place beyond an iron curtain—away from the other struggles for social improvement If it is to fight disease effectively the medical profession as a whole needs in fact to be more than interested in the social services that are fighting the other giants of the Beveridge report Yet what we are actually seeing is a flight by the profession back to the hospital ward the laboratory and the X ray room—where the doctor is isolated from the general life and struggles of the patient as an individual and a member of the community

I have lived long enough to see several attempts made to remove the curtain between clinical medicine, as practised in hospitals and institutions and the person in his home and at work The chair of preventive medicine at the University of Bristol was one of the first to be established in this country and the intention was that it should be a link between medical institutions and the world outside Clearly before such a scheme could function it must offer a service and in Bristol at that time—21 years ago—it offered a laboratory service and the resources of the public health department including X rays for diagnosis in a limited field

Also I was privileged to be a member of the advisory council of the Nuffield Provincial Hospitals Trust, when Sir Farquhar Buzzard, and later John Ryle took up the cudgels on behalf of 'social medicine' Once again the idea was to persuade the clinicians that environment, and in particular its social aspect was of tremendous importance in the maintenance of good health and in the causation and cure of disease

I fear that in neither case has the campaign had a very lasting effect Are not the sympathy and interest of the ordinary man in the quick cure rather than in the long drawn-out régime of prevention? The physician himself is influenced by the attitude of the patient to prevention and treatment and the discovery of the sulphonamides and the antibiotics has made the lot of preventive medicine harder and the glamour of cure even more alluring Indeed, it would appear that the discovery of cures and more cures makes prevention less and less necessary Nature, however, is not as transparent as all that who can venture to say that a cured person, even under most advantageous circumstances, has been completely restored to his pre illness state ? Nor, as I see it, can we ever hope for a 100% cure of all diseases I am convinced therefore that there will be an important task for preventive medicine to face for a long time to come

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* m an address to the conference of the National Association for the Prevention of Tuberculosis, held at Bristol, Sept. 27 1954

### BORDERLANDS

If specialisation must continue and if we are to break down barriers within our profession, as well as between our profession and the others that are trying to make living fuller and healthier, we shall have to develop teams of skilled workers whose activities overlap To the tidy administrator there is no more hideous bogy than "overlapping" It means waste, bickering, discussion, and delay The alternative, however, is an iron curtain or perhaps a gap After many years' experience I am convinced that a certain amount of overlapping between the services is essential if we are to get the best results Overlapping does also mean common interest, with all the advantages of consultations and two or more opinions from different standpoints of the problem under consideration, and the pooling of resources for its solution

For example, though public health and preventive medicine are concerned with the promotion of normal health and the prevention of disease, the boundaries of normal health are very uncertain and the practitioner of preventive medicine should be able and encouraged to diagnose deviation from the normal both in the individual and in the group This borderland of disease is as important to the public health practitioner as it is to the physician or surgeon responsible for treatment This borderland is ground for common interest between public-health and the treatment services Full facilities should be available to both parties in the field of diagnosis overlapping is essential to create common interest, an examination of the problem from the different points of view, and therefore to create better prospects of a solution

The public-health service today is much handicapped by lack of ancillary services to aid it in the detection of "deviation from the normal," and until that deficiency is made up it cannot be efficient The school health, maternal, and child-welfare services would be vastly improved throughout the country if they were encouraged by the supply of most modern equipment needed for diagnosis instead of being handicapped by red tape and confused by legal jargon

My progressive and not too poor local authority has been impressed by these arguments and has purchased, in spite of much obstruction, out of revenue, an X-ray apparatus with a miniature camera It hires out the service to the different sections—school health, maternal and child-welfare, and others In this way we are able to get on with the work without having to worry and wait for the assistance of the hospitals

It is, of course, too true that in the past, when local authorities had more power than they possess today, many of them failed to use it, partly from shortsightedness and partly from lack of funds, but that does not justify the highest authority in the land in acting like an unwise teacher and trying to do the work itself - Surely the aim of our civilisation is to get every person and community—even an elected local authority—to stand on his or its own feet ? A lesson may be learnt from voluntary organisations like the Diabetic Association, [illegible] avowed object is to teach all diabetics to be [illegible] lent as possible

### COMPARTMENTALISM AND TUBERCULOSIS

In spite of treatment tuberculosis remains far too prevalent in this country, and prevention is our chief hope of exterminating it To that end we would all agree that ascertainment—as complete as possible—is the first step, and I regard it as a mistake to erect barriers that will prevent anybody, any organisation, any authority from doing all they can to bring cases of tuberculosis to light There must be publicity and health education, and in this borderland there is room for every kind of organisation to play a part Overlapping in its most extravagant form can never be as expensive in life or cost as the havoc created by this disease

The recent report by a Medical Research Council subcommittee on Mass Miniature Radiography contained arguments which show that the M M R is a valuable arm of the preventive service Yet the conclusions contained no mention of the public health department and the part it should play, and this attitude is supported by the Ministry of Health Surely this preventive instrument ought to be in the hands of the public health department, which has all the advantages of being in touch with the people, to organise and to run as one of its primary duties

This M M.R organisation illustrates the dangers of trying to define rigidly the responsibilities of the different bodies fighting disease and promoting human welfare The practical social workers, doctors, and others must have elbow room to manœuvre The tendency, however, has been—and, one might even say, usually is—for hi course to be set rigidly by the lawyer and the administrator The path of progress is unlikely to be discovere that way—this is a fit task for the free explorer only

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## Arsenic in Food

The Food Standards Committee has adopted th revised report of its metallic contamination subcommitte concerning the limitation of arsenic in foods [1] The genera limits recommended are 0 1 part arsenic per millio in ready-to-drink beverages and 1 0 part per million other foods New limits are suggested for concentrate foods and for food adjuncts which enter the diet only small quantities (soft drinks intended for consumptio after dilution, ice-cream, iced lollies, chemicals used ingredients or in the preparation or processing of foo &c ) The subcommittee also recommends that the sal of sea-foods containing arsenic in excess of 1 0 part pe million should be permitted where the arsenic in ther can be shown to be natural

Before implementing the recommendations the Minister Food has agreed to consider further representations fro interested parties These should be sent to the assista secretary, Food Standards and Hygiene Division, Minist of Food, Great Westminster House, Horseferry Road, Londo S W 1, not later than May 31, 1955

## Influenza

This winter's outbreak of influenza due to the B virus is abating In the 160 great towns of England and Wale deaths attributed to influenza in each of the ten wee from that ended Jan 1 to that ended March 5 numbere 82, 102, 134, 136, 123, 106, 84, 82, 81, and 70, an deaths from pneumonia numbered 380, 417, 471, 55 534, 449, 387, 357, 429, and 449

New claims on the Ministry of Pensions and Nation Insurance in each of the seven weeks from that ende Jan 18 to that ended March 1 were as follows 243,349, 257,091, 232,929, 208,935, 192,396, 193,523, an 208,434

The Ministry of Health remarks that the delayed fa in deaths from pneumonia and the lag in the drop first claims may be due in most areas to the bad weathe rather than to influenza

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[1] Food Standards Committee Report on Arsenic. H.M Stationery Office 1955 Pp 6 4d

[2] See *Lancet*, Feb 5, 1955, p 300

# The Widdicombe File

## XXIII NOLI EPISCOPARI

ar Charles

It was nice of you to write to me about the chair Mingara. No, Charles it's no go Three years ago en it was first advertised, and again now, I can mise you I thought about it most carefully I have ndered this matter I have decided this matter I will ak plain and clear This is my irrevocable judgment m which there is no appeal " I cannot come out to ngara

It hasn t been an easy decision to make As you ow I saw Mingara both in calm and in calamity during e war and acquired a considerable affection both for e place and its people I hanker more than a little er being one of those who

in Khybor or Khartoum
Trimming their nails to meet an east wind
Justify the system

know you badly need a head for the department, and think I could do the job I'm not so sure of a chair in is country—who in this pyramidal profession can be ? that the prospect of hearing myself called Professor is t a very real attraction But I can t do it Charles m *too old* Thirty-eight yes and too old

It s more than a little on my conscience, for I'm nly sure that I'd be doing more good in the world with on in Mingara than snug at *home here at* St. Ethelred s y reasons are I'm afraid selfish ones. But I think it ay be worth airing them for my reasons are those of ry many men who ought to be taking jobs in Colonial versities but won't

You need, as I see it three sorts of people on the ff of a newish Colonial university—the permanents, e locals, and the transients. Permanents like you are blessed indispensable backbone and it would be a ot university that wasn't *beginning to produce* at least few local people good enough for senior jobs But s transients that I'm mostly concerned with here hope you won t regard it as an insult to the other sses if I say that good transients are essential if ra is to remain a live university That s not because opical, or new or because the Mingarans are ish or too much on the make or any such dash It s simply a question of isolation Inbreed t a university is always bad to an isolated univer is fatal Guy's may be too full of Guy s men and of Barts men but at least they meet each other s and even, greatly condescending may sometimes a meeting at Ethelred s. Even in this bandbox island the *medical* schools which are furthest their neighbours—Aberdeen, Newcastle Bristol to make a more definite effort to keep in the swim h is not to say they don t make it) than *London* or Manchester Mingara is 2000 miles, more from the next medical school and even in these of the Comet (alas, that our comet has had its tail d) that is a long way and even worse an expensive to drop in to hear an interesting paper or discuss mon problem.

isolated school must rotate a *substantial part of its* with other universities if it s not to stagnate tical years visiting professorships travelling ships—all these help but nothing can replace the infusion *of* new blood The advantage isn t we benefit greatly by the return of those e seen a different-coloured world at close quarters you get better that will count *for* more and But what is merely good for us is life itself for you this country s not your only source are mostly too expensive and Europeans talk the wrong languages but there s the rest of the Commonwealth You ll exchange of course with other Colonial universities and most of the Dominions are open too —*isolation is just as much of a problem with lots of the* Dominion universities as it is with you, though they only sporadically realise it And so far as we are concerned, there are several independent countries—mostly Middle Eastern—where we used to fill medical teaching posts and where (judged by persistent advertisements) we are still wanted and won t go

Why won t we go ? Why specifically won t I come to Mingara ? You offer me a reasonable department, a superabundance of research problems a job well worth doing and with it a very adequate wage a climate the kids would revel in and a release from the washing up and all that goes with it. (Beatrice is scared of native boys, but it would be no end good for her )

Basically it s very simply this *How do I get back ?* I could serve you *optimally* for five or six years—perhaps eight at the most It would be wasteful to go for less. After six years it would be time for me to leave my out post let a fresh mind take over and come home to have a little of the self-conceit knocked out of me (it affects different people in different ways but I know that if I was the only accepted fountainhead of knowledge of my subject for a thousand miles my head would swell insufferably) Moreover the kids would be by then in boarding-schools in England, and Beatrice would be *itching to be home beside them*, and all the worst features of life in the tropics would be emphasising themselves to us. So for your sake and my sake equally I ought to come home But what to ? What job could I count on coming home to ?

It is I think literally true that there isn t a single chair in a medical subject in this country held by anyone who's previously held a Colonial chair—outside tropical medicine (and I know of only one in that even) If there are any exceptions they must be very few Now I *presume—and I very much hope I am right in presuming* —that you'd not appoint me to a chair in Mingara unless you thought me good enough to hold a chair in this country or anyhow likely to to be good enough in a few years' time But if I come out to Mingara, it seems that only exceptional good luck will get me back where I started 2/i/c of a teaching department, and that I will be fairly lucky to get even a decent non teaching hospital consultant post. Competition is keen and the best jobs go to those who ve stayed on or near the spot

It is one of the paradoxes of a progressive profession that the buckets that leak fastest stay fullest The faster one s young men rush off to better jobs elsewhere the faster others throng to replace them Even in chairs there is a hierarchy : no one minds starting at the bottom of the ladder but no-one willingly chooses the ladder with no top to it

*What s to do about it ?* Things will get better as you get more established and as the influence of the war (which has made teachers mature older and so less mobile) recedes and as we get more overcrowded And you will always get the few idealists and eccentrics who come out just because they shouldn t Much of the best work in every science is done by idealists and eccentrics but a stable department let alone a whole medical school needs a fair stiffening of good solid family types. (Isn t it odd though to be irrelevant for a moment how often people belie their *social casting when it comes* to the quality of their original work ? Provocative ideas come from Tory clubmen with very old-school ties meticulous techniques from long haired musical Sephardim destructive criticisms from family men with contented homes flashy stuff from dour Yorkshiremen and sound work from spiv cockneys—and wouldn t life be dull if they didn t ?)

My own (partial, admittedly) answer is a massive extension of seconding It's easy in theory, though not always in practice, to get seconded abroad from a British university for one year, possible for two, but impossible practically for more than that It should be possible for a man appointed to a Colonial chair, or any post of public importance overseas, to be seconded from his home post for, say, six years He could put his shoulder to your wheel then with no carking care for the future, with no half-eye, in all he did or wrote, to a distant selection board He could come home to a job perhaps less than his desserts, but at least something he has not to scramble for At least it will give him time to look about him If he was worth the appointment in the first place, and if he's used his time to a good purpose since, he should be able to climb further The difficulties of the seconding school in such a course can't of course be laughed off entirely, but I believe that with good will on both sides there's nothing insuperable Let it be done successfully once, and it would be easy for half the battle in such a scheme is the confidence that it's workable

I would like to see tried an even more fancy scheme in which two men of roughly equal status are appointed together to two posts, one a Colonial chair and the other a readership at home They would alternate between the two at say eighteen-month to two-year intervals, swapping houses and research projects, and looking after each other's children and other interests, and generally playing Cox and Box as much as possible Thus one might get the maximum of continuity with the minimum of stagnation The original pair—and their wives—would have to be young, tough, adaptable, and infinitely tolerant of each other's troubles but they would have enormous fun and might well do great things Impossible? How do you know till it's been tried ?

No matter what the solution, I must confess that one root cause of your troubles is one that I'd hate to see eradicated For all our beefing (and why not ?—for love of research implies dissatisfaction with the existing order, and so all scientists are grumblers at heart) there's a lot to be said for academic medicine in this country The University Grants Committee may walk a tight rope, with the stifling net of Government control (or the hard cold ground of bankruptcy) to catch its least stumble, but so far it's balanced supremely skilfully and it shows no sign of falling yet So long as it works, universities in this country remain as free of non academic influences as any in the world We're no plutocrats, but we're paid probably nearly as much as is good for us The pace in research is hot but not killing, and man for man we pull our weight I think as well as any Perhaps it won't last perhaps we will become Civil-Service minded, and perhaps it's true we're attracting a less original kind of student and will suffer in the next generation (but haven't students always been worse than their fathers ?) Myself, I like it here, and here I intend to stick

Am I too easily satisfied ? Do I sound to you like the Reverend Eli Jenkins, whose lovely lyric in Milk Wood is after all, when you boil it down, no more than sentimental parochialism ? I'd rather sing to you in the words of the early Keats

> 'Happy is England ! I could be content
> To see no other verdure than its own ,
> To feel no other breezes than are blown
> Through its tall woods with high romances blent ,
> Yet do I sometimes feel a languishment
> For skies Mmgaran "

But I am, as I said, and as it should by now be obvious, too old I'm sorry, Charles You'll soon find someone better than me

Yours,

PETER DAVEY

# In England Now

*A Running Commentary by Peripatetic Correspondents*

HOWEVER long the sentence, the full stop at the end is always the same size Alas, one cannot say the same about the last patient His size grows with the latenes of the hour and the number that have gone befor him

At routine medical examinations the last applicant will have covered his form with illnesses which he refuses to have dismissed as minor Nothing but a detailed inquiry into hi history will satisfy him Any sign of impatience will bring forth "Well, doctor, it does say *any other illness*, and I always say it pays to be honest" The extraordinary thing is that not only does he have a long history, but also a heart murmur and a trace of sugar in his urine When all is over and release is in sight, as your hand steals towards your pocket to light up another carcinogen, he turns as he goes through the door and remarks "Of course I did once have a nervous break-down, but that's not really a disease is it ?"

At the end of Outpatients the scene is different ye the same Glancing at the notes of the last patient i seems that it will only be a case of "rep mist" But a the patient enters with that firm, determined gait anxiety is aroused, and as she sits down firmly, arrange her belongings around her, undoes her coat, throws bac her scarf, removes her hat, and pats her hair, fear grip you This apprehension is immediately confirmed as sh opens the proceedings with "I'm afraid your medicin hasn't suited me at all Not only is my pain still there but I have now developed "

In general practice you may meet the last patien either at the end of the round or at the end of surgery The aura, which occurs after examination and treatmen of the patient, consists of a short introductory phras followed by the euphemistic use of a rhetorical questio thus—"Oh doctor, while you are here, would you min looking at "

Surgeons tell me that the last simple appendix alway has adhesions and that the last tonsil always keeps o bleeding

Even in the Services the syndrome can be observe I remember one evening at about five to five, just a I was climbing into my greatcoat, the sergeant rushe into my room

"Going off, Sir ? There's just one more"

"Tell him to come to morrow, or if it's urgent get the du doctor"

"He insists on seeing you, Sir"

"Who the hell does he think he is—the Air Offic Commanding ?"

"That's right, Sir"

* * *

I was having dinner with my aunt when she plunge her hand into her bag, extracted a letter, and passed to me saying "I thought you might be interested" was a note from a consultant to her G P "Very nice I said, "but how did you come by this ?" "Have been naughty ?" she asked "When I went to m doctor the receptionist gave me my record envelope take in to him, and while I was waiting I found th in it, and I thought you could explain it to me Perha I *was* naughty, and now I'm rather worried in case h misses it"

My wife, who knows the answer to most question solved this one "You go along to him to tell him ho much better you are, and when the receptionist giv you your card, just slip the letter back, and he not know"

So she did, and he didn't

* * *

The taxi-drivers of New York are an articulate an mostly intelligent race As soon as they found th I came from this side of the Atlantic, they would ope up and give me their views on diverse subjects M Chamberlain, his umbrella, and his trip to Munic came in for much adverse comment On the other han Mr Roosevelt and Mr Eisenhower did not make a ver ood showing According to the taxi-drivers, the country ent to the dogs under Roosevelt, and under Eisenhower, gathered, the States are putting on an act rather like hat of the Gadarene swine Being in possession of a si-diplomatic visa I felt it my duty to protest and oint out my great admiration for the people of the United tates, their potentialities and their accomplishments alike Carlyle, I was unable to hide my affection for the ople of that great land. But the taxi-drivers would ave none of it 'You just don t know the half of it, ey said. Look, said one, at our juvenile delin ency! , and he went on to explain that, in his ion, juvenile delinquency came in with child psycho- gy "It was a bad day,' he said, when the principle f not thwarting or punishing was put forward Take gs. To train them you have to hurt them a bit Then ey remember not to do it next time. I was able o slip in quickly a remark about Pavlov and the nditioned reflex. He seized on it. That s swell, and m going to use it next time I talk about juvenile linquency By this time we had reached Penn Station here we parted with mutual expressions of good will must admit that I grossly overtipped him A kind of tertainment tax

* * *

For the first time ever we were the successful candidate the interview As we peripatetted happily back in e general direction of the Northern Kingdom, in our ry first car—bought on the strength of the interview recently and satisfactorily concluded—the Northum an night grew ever darker, wetter and wilder, the coming lorries more and more numerous and their adlights more and more blinding Our own grew ever ebler and at last succumbed We were forced to call a lt until we could continue our progress by daylight. t what a fortunate stopping place a few more miles the darkness, and we should have missed the find of e year the solution of a major medical mystery You y find it in the literature, there for all to see The refer- ce is 893/039 O.S Quarter-Inch, Sheet One (The rth, Chessington 1940—no less than the whereabouts that ubiquitous and omnicompetent writer Etal

* * *

Will the Back to Victoria movement now filling our shelves and flooding the antique shops with painted l-scuttles, bamboo curate s joys and red plush table- ths with bobbles soon affect our own profession? ll we hear, across *hospital luncheon tables* so hibited an egg in port wine *per rectum* " through courtesy of Dr Shufflebotham, the family practi ner After hearing the history and after examina of the patient, I decided he was suffering from '? es will of course prosper and riddles return:

*onsultant on ward round* Riddle-me-ree!'

*ouseman eagerly*: Not *another* one, Sir?

*nsultant* "Yes, m'boy Why is the N.H.S like a e at lawn tennis? You give it up? Because though may have a good Racquet you ll be taken to Court though you Love it to begin with at Forty it may be the ." (*Whereupon the Houseman is so consumed with ment that he drops two cups and a seton and allows a escape into the bed*)

* * *

In Scotland at present many of my colleagues who are ts are behaving oddly They have a far-away look ked a question they tend to reply in snatches of mpare terms of x and y or the coefficient of ssion. Instead of knocking impatiently at the oom door in the morning they give precedence to progeny They make anxious inquiries about the tion of pens pencils, &c In brief the 'Highers' more upon us.

e of my offspring whose intellectual processes tion by a kind of leapfrog mechanism, was confronted a biology question on plant fertilisation obviously nding a ladylike discourse about pistils, stamens, pollen in the appropriate *setting of a sunny garden* s in bloom, and the hum of the bee tribe. Instead chose to write on the joys of muck spreading and two foolscap pages she wallowed in the rich effluvium farming. Does she get a credit?

# Letters to the Editor

## HYPOTHERMIA IN THE NEWBORN A NEW SYNDROME?

SIR,—Comparatively little has been written of the dangers of heating small premature infants and your annotation of March 5 is most timely, especially in this age of incubators

In 1953 at a meeting of the section of pædiatrics of the Royal Society of Medicine when the effects of environment on the premature baby were being discussed I drew attention briefly to a refrigerated state occurring in these babies and emphasised the danger of warming such infants too quickly[1] I mentioned that pneumonia which had not been detected clinically, was the usual post-mortem finding Further experience at the Royal Alexandra Hospital for Sick Children in the last two years has shown that this remarkable syndrome although confined to the early days of life is by no means peculiar to the premature infant indeed the 4 examples we have seen in the last few weeks have all been in babies with a birth weight above $5^1/_2$ lb

I feel that it is especially important for doctors and midwives concerned with domiciliary work to be aware of this disorder

The syndrome as I have seen it is almost confined to babies born at home during the winter months. Birth is usually uneventful and the child behaves normally for a few days. Refusal to feed and increasing lethargy and coldness are the most constant presenting symptoms. On admission to hospital the infant feels cold and indeed radiates coldness; the extremities and face—particularly the eyelids—are puffy and pitting œdema, at times gross, may be demonstrated in these places some associated induration of the skin may be present (scleroedema) but this is certainly not a constant feature at this stage The baby lies motionless and respiratory movements may be difficult to discern The most striking and constant finding (and one liable to mislead) is the unusual pinkness of the cheeks, chin and lips, and sometimes the eyelids.

Attempts to record the baby s temperature on arrival at hospital using an ordinary clinical thermometer are unsuccessful A low reading thermometer commonly gives a rectal temperature of 80–90 F but this figure recorded in the admission room and usually after some heating at home or during the ambulance journey may be appreciably higher than that which obtained when the baby first became sick. The rectal temperature of the most recent case we have seen was 74°F; and this baby was swathed in blankets and was 3 feet from a fire and extra heat was being provided with the help of a hot-water bottle when I saw it at home

As far as treatment is concerned I can be quite definite about one thing that injudicious heating leads to death in a few hours cyanosis and sometimes convulsions being terminal features Even the ordinary ward temperature may be too high for nursing purposes and we have found it necessary in the last month to open a special cold room ' to avoid a too rapid rise of body temperature and consequent anoxia At the moment we keep these babies cool for their first few days in hospital, thereafter allowing their temperatures to rise slowly

Since the most constant necropsy finding is pneumonia, usually hæmorrhagic, an antibiotic is given by way of the alimentary tract where possible through an indwelling 'Polythene tube 3 of our 4 recent cases have developed profuse purulent nasal discharge within a few hours of admission and this complication may make inadvisable the passage of a tube through the nose

Intermittent œsophageal feeds the tube being passed through the mouth may then become necessary since these infants are quite unable to take food from a bottle or spoon It has been our practice until recently to give full-strength breast milk feeds from the time of admission; but in our most recent example of this syndrome complete anuria has complicated the picture and made feeding difficult  Although it seems rational to provide calories for the maintenance of body temperature it must be remembered that most of these babies are œdematous and further water retention must not be encouraged  In our experience oxygen therapy does more harm than good  But if cyanosis appears, oxygen must of course be used

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[1] *Proc R Soc Med* 1953, 46 883

Although post mortem studies suggest that an underlying pneumonia is a constant accompaniment of this hypothermic syndrome, physical signs in the chest do not indicate consolidation  Added sounds over the lungs originating in the upper respiratory tract are a common finding  One of our recent cases, now recovering, had a normal chest radiograph on admission  A second radiograph forty-eight hours later showed consolidation of the right upper lobe which might have passed undiagnosed if this early repeat film had not been taken

A more detailed report is being prepared for publication  It would be interesting to hear if others are seeing examples of this syndrome

Royal Alexandra Hospital
for Sick Children, Brighton
TREVOR P MANN

## SANATORIA

SIR,—Your correspondents' views seem to range from those, like Dr Stradling (Feb 19), who think sanatoria are outmoded to others, like Dr Snell (March 5) if we read him aright, who think they should form the basis of tuberculosis treatment and that the general-hospital beds now used by chest clinic physicians should be put to better uses  As chest clinic physicians who still believe that the sanatorium has a place in the treatment of many tuberculous patients, we feel that the latter is not the whole answer  We think that sanatorium physicians take perhaps a too one sided view  For many years they have taken the cream, as it were, of the tuberculous patients—i e, those with a relatively good prognosis  They have been insulated from the problem of the considerable numbers of chronic advanced cases treated by the chest-clinic organisation

Leaving aside the other uses to which the chest clinic physicians put their general-hospital beds it is difficult to see how the sanatoria could readily deal with such cases  Many patients are elderly, they dislike going to hospital and will only do so for short periods and provided it is not too far away from home  They are subject to frequent intercurrent infections and often need all the resources of a general hospital  As a rule they are not too welcome in sanatoria, which can at most bring them only to a stage of "maximum benefit" from which they commonly relapse  The control and treatment of this army of "chronics" is a matter in which the chest clinics can at present get only a limited amount of help from the sanatoria

Ealing
GEOFFREY BEVEN
HUGH CLIMIE

SIR,—Your timely leading article[1] has given rise to a useful correspondence  I think it important, however, that we should clearly maintain the distinction between "sanatorium treatment"—the principles of treatment laid down these many years as the basis of sanatorium therapy—and the transference of the patient bodily from the associations of home and relations and friends to the remote geographical location designated a sanatorium  In the principles of sanatorium treatment we all believe, but over the admission of all tuberculous patients to sanatorium there is wide divergence

In deciding whether to recommend admission to a sanatorium we must weigh, among other factors, the value of prevention of the disease, and recognition of the patient as an individual

Prevention involves good housing, good food, fresh air, and good ventilation, and the removal of the infected person from close contact with healthy relatives  Some claim that prevention is best achieved by removing the patient to a sanatorium, there to enjoy "peace and quiet"  But others point out that in such a selected and segregated population all the patients are likely to be equally distraught and uncertain, and claim that, given an adequate level of housing, the health visitor, chest physician, and family doctor, with the coöperation of the relatives, can successfully prevent the spread of the disease without the patient being removed from home

Secondly, it should be remembered that man is not the flat citizen of flatland, nor entirely a "rude mechanical that works for bread"  Tuberculosis is a disease of the whole body focused on one or more organs, and if we are to enable the patient to overcome the infection we must treat him as an individual  He should be placed in the best possible environment to attain "courage, gaiety and the quiet mind", and while admission to sanatorium supplies this for some, the surroundings of home and family are the ideal setting for many more  To suggest that sanatorium provides the ideal surrounding for mental and bodily rest and that only a small psychological adjustment is necessary on return home is nonsense  The interminable discussion on phases of the disease and modes of therapy that result from enforced segregation in sanatorium produce the tuberculosis complex of living tuberculosis, thinking tuberculosis, talking tuberculosis, and even dreaming tuberculosis, while "barrack room lawyers" commonly produce a state of mind that destroys the will to coöperate in treatment

The treatment of tuberculosis should be a planned combined operation  If the planning is sound, then I submit that the number of patients admitted to sanatorium will continue to decline

Maidstone
D L PUGH

## MENTAL HEALTH AND SPIRITUAL VALUES

SIR,—Psychiatrists and many others must feel a debt of gratitude to Sir Geoffrey Vickers for his address, so erudite in content and felicitous in presentation  In the abridged version, which appeared last week, he raises, however (p 524, paragraph 2), points which seem to merit comment  He writes

> "Yet a conflict is not necessarily resolved merely by being disclosed  It may not be capable of being resolved, it may simply have to be borne  Tensions are not only inescapable but necessary and fruitful  It would certainly not be fair to say that psychiatry offers escape from them, while religion offers the strength to bear them, for each in some measure offers both, but the emphasis in psychiatry and throughout the field of mental health is on reducing rather than on supporting stress"

The reason why psychiatry favours reduction techniques is, surely, because neurotic tensions are, by and large, escapable, unnecessary, and fruitless

Patients oft times asseverate  "Had my religion been valid or my ethics sound, I should not have required medical assistance"  Many such folk are deeply religious and morally sincere, they are in the grip of tensions they wot not of  Resolution of conflict, simply, places them in the position of the healthy, but since neurotic conflict hinders development, and is in effect always of long standing, immaturity is, in addition present, and helping patients to grow up is the second essential of psychotherapeutic procedure  This aspect has, certainly, a spiritual connotation

The implications seem to be  neurotic conflicts differ—qualitatively—from the tensions of progressive life  If accuracy is to be achieved, psychological facts derived from psychiatry require to be subjected to criticism before being granted œcumenical status  The present is no more an age of neurotic anxiety than any other  Current conditions, however, favour the development of objective anxiety  Most people, in tension laden communities, are, on the one hand, warm and well fed  They are, on the other hand, constantly reminded of the devastating potentialities of atomic warfare

London, W 1
MURDO MACKENZIE

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[1] *Lancet*, 1954, ii 1313

## CEREBRAL ARTERIAL DISEASE

SIR,—Your annotation of Jan 15 commenting on our ent papers,[1] questions our conclusion that cerebral ery aneurysms of the berry type may arise on other n a congenital basis.

Fundamental to an understanding of the pathogenesis certain types of vascular lesions is the fact that the ious components which make up the walls of arteries capable of only a limited range of tissue response to rious agents, so that the same lesion (sclerotic plaque aneurysm) may develop from unrelated causes.

timal elements can respond by an increase in ground stance and by the proliferation of fibroblasts to produce initial phase of plaque formation. The internal and ernal elastic lamellæ, which degenerate by fraying fibrilla n, fragmentation, and granulation may respond by uplication of existing elements or by the new formation elastic tissue; additional support may thus be gained by new formation of elastic fibrils in the intima and media well as along the internal and external zones Degenerated d destroyed muscle may be replaced by fibrous tissue ents, and the limited response potential is expressed only the form of hypertrophy of spared muscle fibres Finally interniz, Thomas, and LeCompte[2] have shown there be increased vascularisation of the artery wall

Furthermore the tissue response of a particular artery also limited by its initial structure Cerebral arteries handicapped in that they lack an external elastic ella or have only a rudimentary one and are thus thout a protective mechanism afforded arteries else ere This weakness makes them more susceptible to urysm formation than are other arteries of com able size Both Forbus[3] and Glynn[4] make the point t, despite the defect in the muscular coat aneurysms not form in cerebral arteries unless the internal elastic ella is injured and Eppinger[5] has observed that urysms are rare outside the cerebral circulation ough, muscular defects similar to those in cerebral ries are not uncommon elsewhere

The difference in tissue response potential between ries in different locations may be further illustrated other comparison In cerebral arteries inflamma lesions may result in aneurysm formation as recently rted by us,[1b] although we do not contend that this only mechanism by which elastic tissue may be ed and an aneurysm may be formed In coronary ries, on the other hand similar inflammatory lesions to stenosis with narrowing of the lumen as illus d in the excellent article by Zak Helpern and nberg[6] Similarly as regards arteriosclerosis the genic processes which in coronary arteries produce wing lesion with eventual occlusion of the lumen in cerebral arteries lead to aneurysm formation or —events which are very rare in coronary vessels iticism that in our work the arteries were not in a state of distension to normal pressure is not a one since without resorting to this technique we able to demonstrate frequent bulging of plaques the media; and in fact we explained this tendency bral arteries as due to lack of the protection usually ded by the external elastic lamella

light of these observations it appears fruitless to that congenital defects play a primary rôle in the opment of cerebral artery aneurysms There is some question as to the congenital origin of muscle ts which, so far as we know, has not yet been established The occasional association of these defects with other congenital lesions may in fact be fortuitous since the large majority of cases exhibiting them do not have other associated congenital abnormalities More pertinently it seems clear that greater protection is afforded by elastic elements than by muscle

We may add that in our opinion the importance of circulating lipids in the causation of plaques has been greatly exaggerated We recognise that primary atherosclerosis can develop on the basis of elevated serum lipids in certain definite clinical states including familial hypercholesterolæmia hypothyroidism and lipoid nephrosis but to what extent this happens under other conditions remains to be established Our investigations are aimed among other things at determining how far the appearance of lipids in plaques is due to local degenerative processes within arterial walls

The Jewish Hospital
St Louis
Missouri U S A

HERMAN T BLUMENTHAL
FRED P HANDLER

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H Arch klin Chir 1887 35 1
Helpern M. Adlersberg D Angiology 1952
C. R. Arch. Path 1933 16 630

## AIR EMBOLISM ASSOCIATED WITH RUPTURED UTERUS

SIR,—My interest in the article by Mr Scrimgeour and Mr Carrick (March 5) is related to experience of accidental air embolism during therapeutic injection of air in artificial pneumothorax and pneumoperitoneum Additionally my wife suffered a minor air embolism some years ago after a normal delivery and this was diagnosed at the time by the occurrence of faintness dimness of vision, and severe pain between the scapulæ lasting for about half an hour

As students we were taught about ' pleural shock " which is now generally acknowledged by chest physicians to be due to air embolus and it would seem that some cases of obstetric shock may be due to the same cause

The first aid treatment of this condition, which may be life saving is immediate lowering of the head, even to suspension by the legs and preferably with rotation to the *left side* This presumably allows the air to float away from the brain and heart to the lower part of the body where it is gradually absorbed Since the air must enter per vaginam it would seem reasonable to occlude the introitus with an air tight pad after delivery of the placenta.

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London, N W 9

W E SNELL.

## INNOCUOUS TEMPORARY IMMOBILITY

SIR—Dr Rudolf (Jan 1) states that 19% of 60 male *and female* nurses whom he questioned had had one or more attacks of night nurse's paralysis or as he prefers to call it, ' innocuous temporary immobility '

I found that of my small staff of five European nurses the four who had been trained in England all knew of the condition, and two had experienced it personally while on night-duty during training One nurse had had it twice the other once and all three attacks had followed the same pattern—i.e inability of the nurse who had been sitting relaxed in a darkened ward to rise from her chair on the approach of the night sister

Is Miss Peace's disability[1] really an example of the above condition? There seem to be certain features which relate it rather to sleep paralysis '—the relative *frequency of the attacks* auditory hallucinations and the feeling of unreality which indicates a dream state on the verge of sleep

I have under observation a middle aged man who for some years has had attacks of ' sleep paralysis

These attacks are accompanied by anxiety and a feeling that he must force himself *fully* awake and sometimes by auditory hallucinations such as high pitched music *or* the voice of an acquaintance Once he had a strong impression that some one was at the front door; he imagined he heard his wife say, "That must be Mc—", he did not catch the name but the rest of the sentence was so clear and distinct that he rejected the idea of an hallucination and thought "I really am caught in this ridiculous situation, by a stranger, this time"

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[1] *Lancet* 1954 ii 1354

It would be interesting to learn whether Miss Peace has ever had episodes of irresistible sleep, or of sudden muscular flaccidity under the influence of emotion, both of which are experienced by my own patient

Is it too far-fetched to suggest that such brief muscular immobility in man may depend on unrealised conflicts of impulses, which in a simpler form—that of conflict between the impulse to seek safety by running away and the impulse to stay and protect the nest—underlie the "injury feigning" or "distraction displays" of birds?

RHODESIAN DOCTOR

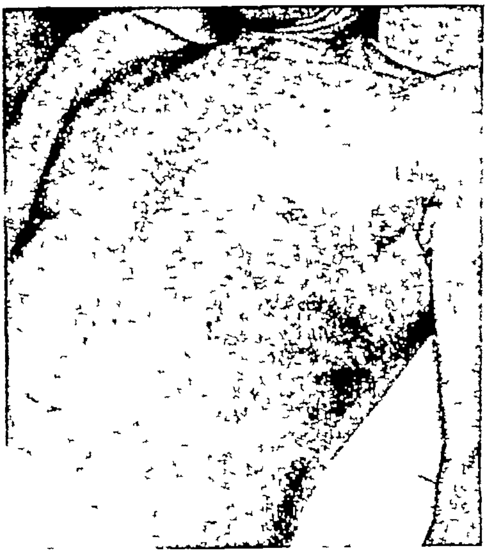
## DISSECTING ANEURYSM OF THE AORTA

SIR,—We read with great interest the account by Professor Thomson and Dr Marson (March 5) of two cases of rupture of aortic dissecting aneurysm causing subcutaneous hæmorrhage We have recently seen a patient with a similar condition who survived in hospital for twenty-three days

A labourer, aged 61, complained of sudden severe pain in the left shoulder, while engaged in his usual occupation of shovelling gravel The pain quite rapidly subsided to a dull ache and he was able to complete his day's work That evening, however, he noticed that a large bruise had appeared over the left side of his chest, and it was on this account that he came to hospital. On admission the patient had no other complaints and there was no history of previous illness

On examination, his general condition was good There was extensive subcutaneous bruising along the inferior and medial border of the left pectoralis muscle, and the whole of this muscle appeared to have been lifted forwards The left radial pulse was weaker than the right, and both were collapsing The femoral and carotid pulses were equal The left external jugular vein was distended. The heart was not enlarged on clinical examination, but there was a loud aortic diastolic murmur Radiographic examination showed a large soft-tissue swelling of the left chest wall and some broadening of the aortic shadow An electrocardiogram was normal There were no other abnormal findings.

The bruise, while slowly fading, spread to the flank (see accompanying figure) The patient's condition remained good but after twenty three days, while still in hospital, he suddenly died


Bruising of chest wall and flank.

At necropsy it was obvious that the immediate cause of death was hæmopericardium. In the ascending aorta there was a [illegible] tear, 2 cm long, in the intima, from which a dissecting aneurysm could be traced that involved the arch of th aorta and the left subclavian artery The point at whic the aneurysm had ruptured into the tissues could not exactly defined, although it seemed to be in one of the branch of the subclavian artery deep to the pectoralis major Histological examination of the aorta showed the characteris cystic necrosis of the media

Green and Saphir[1] described the case of a wom with a ruptured dissecting aneurysm of the aorta and su cutaneous ecchymoses of the lower abdomen, who di within thirty hours from the onset of symptoms similar case report has been found in the Engli literature

M G FITZGERALD
E J WATSON-WILLIAMS

Medical Unit
Cardiff Royal Infirmary,

## ADENOTRIPHOSPHATASE IN HERPES ZOSTE

SIR,—During recent research with compounds the phosphatase group in the treatment of herpes zos I have found that adenotriphosphatase (10 mg per given subcutaneously at the site of the pain) has relatively rapid soothing effect

At each injection 1 ml was given, and in no case w more than three injections necessary These were given consecutive days when the condition did not clear up rapi with gradual desiccation of the lesion and uneventful recov So far 10 cases varying from mild to severe and exten herpes zoster have been treated by this method and all h responded rapidly

It is improbable that adenotriphosphatase has anti properties Its effects are probably due to some biochem change with abolition of an antidromic reflex It seems this action is specific and not due to the introduction o foreign protein. The adenotriphosphatase was prepared fr potatoes by the usual method

Adelaide, South Australia

MICHEL BROUS

## ENURESIS

SIR,—I must congratulate you on your leading art of Feb 19 In particular you wisely emphasise physical and mechanical causes, which are less freque recognised than the psychic overlay

Certain fundamental facts deserve to be still furt stressed Neither diminished bladder capacity excessive nocturnal excretion of urine can alone ca wetting What is important is the relationship of one to the other Night wetting occurs when the vol excreted at night is greater than the bladder of particular child will hold

This relationship may be expressed by a ratio, the "n urine/bladder capacity (N/B) ratio," which is defined as mean volume excreted at night (between 8 P.M and 8 A divided by the mean of the volumes passed in each ac micturition by day This ratio gives the number of times bladder is comfortably filled in an average night In contr children the N/B ratio is not greater than 2—that is to the bladder will contain during sleep twice its mean du capacity In the vast majority of enuretics (80% of consecutive patients) the ratio is higher than this—o as high as 4 or 5 or more

Having established that the bladder is filled with u several times each night, it remains to decide whether bladder holds less than it should, or whether the night u is excessive, or both, and then, after assigning the c blame to one of these factors, one must try to find the c of the abnormality Of course the bladder capacity we measuring is purely functional, and any residual urin excluded from it

It appears from my figures that the functional capacit a normal bladder is loosely correlated with the volum urine excreted during the day time Apparently the times evacuation of the bladder are determined to some extent outside influences—by the parents, by the school rout by imitating companions, or sometimes by the direct or of the teacher who insists on her younger pupils passing at set times The intervals between acts of micturition b thus determined, the healthy bladder develops a capa adequate to the volumes it is called on to hold s it is found that children who excrete a normal daily t of urine, but an unduly high proportion of it at night o excrete less urine than normal by day, and therefore e a somewhat reduced bladder capacity On the other children who have an abnormally high total output y day and by night are nearly always found to have a unctional bladder capacity In such children nocturnal s occurs only when the volume excreted exceeds the y of the normal bladder to compensate for it by expan and in such children there is always diurnal frequency r day wetting as well.

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[1] Amer J med Sci 1948, 216, 24

e following expresses very approximately the on for many children A normal child excretes han half as much urine in the twelve hours of the s in the twelve hours of the day He can if he , contain his urine for half the day and therefore n hold it for the whole of the night If, as the result ease, accident, or heredity, he passes three quarters uch urine by night as by day, he will be able to in his urine through the night only if he can hold r three-quarters of the day A healthy bladder can ve this with training If he excretes equal volumes ay and by night, he will be able to last through the t only if he can last the whole day Although this sometimes be achieved by bladder training alone, eneral every ancillary aid must be brought to bear uch children including waking restriction of fluids s, and the nocturnal bell ringing device

erbridge, Surrey  E M. POULTON

## YPERSENSITIVITY TO PRIMARY AROMATIC AMINES

ir,—May I comment on the letter by Dr Joseph nes and Dr Elizabeth Barnes in your issue of 26

They remark on the puzzling apparent inability of tain aromatic amines (p aminobenzoic acid sul amides, and procaine compounds) to produce the dular fever like condition which can be caused by r primary aromatic amines.

This curious specificity is, of course very puzzling but it is the characteristic feature of such drug hypersensitivity tions—for example the reaction to aniline but not to inobenzoic acid [1] the reaction to acetylsalicylic acid not to salicylic acid [2] and the strong reaction to 1 3-di oxybenzene but the weak reaction to 1, 2-dihydroxy ene [3] Although a primary aromatic amine structure be the basic structure necessary for a hypersensitivity tion to occur whether or not the reaction does occur with what intensity the reaction may proceed is likely be greatly influenced by the presence of other structures aromatic-amine molecule [1] It might even be that additional structures would create an absolute barrier igenicity possibly by blocking the molecule s protein ing power Whether or not this is so it seems that we ertainly expect the pattern of hypersensitive reactivity ated chemical structures to vary from patient to patient perhaps in the same patient at different times

seems to me that the importance of the letter by es and Barnes lies in its concept that the clinical festations termed glandular fever may represent mmon end pathway syndrome activated by an e mechanism

is seems an important consideration because it often ars to me that it is taken for granted that glandular or "infectious mononucleosis is a precisely defined e with an established virus ætiology In practice of many hæmatologists find its ill-defined nature most ling, especially when considering the motley assembly parently infective glandular fevers which appear hin the realm of general practice and also the apparent extensions of the syndrome into other disease-entities as the Reimann type of chronic agranulocytosis with ernating lymphocytosis, monocytosis, and eosinophilia.

In view of these difficulties, might it not be better to cease speaking of glandular fever and infectious mononucleosis as though they represented a precise disease entity with a single specific ætiological background and instead speak of the "glandular fever syndrome" Although, no doubt, this would be of little immediate practical assistance, it might remind us of the probably variable basic (possibly allergen) mechanisms at play, whether they be virus (e g infective hepatitis) bacterial (e.g , *Erysipelothrix monocytogenes*) protozoal (e g toxoplasmosis) or chemical and eventually this reminder might assist in the tidying up of this hæmatological ragbag The idea of a mixed ætiology for glandular fever is not new [4] but it has been sadly neglected

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## CHLORPROMAZINE

SIR,—Last September we described the results of intravenous infusions of 25 mg chlorpromazine on hand blood flow [5] Because considerable vasodilatation was produced after introducing 0 1 mg adrenaline per min into the brachial artery it was inferred that "reversal" of the adrenaline constrictor effect had occurred

Although subsequent studies with Dr R S Duff and Dr Jean Ginsburg have confirmed that chlorpromazine is a powerful vasodilator and has a quite definite 'blocking' effect on the local constrictor action of adrenaline, it has not been possible to confirm a true adrenaline reversal effect on the skin vessels It is hoped shortly to publish the results of these further experiments

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C A FOSTER
E J O'MULLANE
H C CHURCHILL-DAVIDSON

## VENTRICULAR FIBRILLATION IN FALLOT'S TETRALOGY

SIR,—The following case seems to merit a brief report because of two features of particular interest firstly, the rarity of ventricular fibrillation in Fallot's tetralogy, and secondly the beneficial effect which appeared to follow the administration of procaine amide ('Pronestyl')

The child, aged 10 months and weighing 27 lb , had been grossly cyanosed since birth and she was having frequent severe cyanotic attacks There was a palpable right ventricular impulse and a blowing systolic murmur in the pulmonary area and the second sound was single. A diagnosis of Fallot's tetralogy was supported by electrocardiography and fluoroscopy

Cardiac catheterisation was performed under light general anæsthesia, induced with 1·4 ml of bromethol rectally and continued with small amounts of trichloroethylene Atropine was given as premedication. A no 6 catheter was passed via the right median basilic vein to the right atrium and then quickly through the right ventricle (pressure 80/0 mm. Hg) into the aorta. As the tip entered the aorta the cardiac rhythm changed suddenly to ventricular fibrillation. The catheter was immediately withdrawn to the superior vena cava and procaine amide was drawn up ready for use After about 30 seconds the rhythm changed to ventricular tachycardia; spontaneous breathing continued but no pulses were palpable About one minute after the onset of the arrhythmia 100 mg of procaine amide was given down the catheter and 30 seconds later there were five beats of supraventricular origin with an immediate return to the ventricular tachycardia A further 50 mg of procaine amide was then given by the same route There was no immediate effect and the dose was to be repeated when there was a sudden reversion to normal rhythm which was maintained Recovery of consciousness was entirely normal As soon as the arrhythmia occurred the anæsthetist began to give 100% oxygen.

The electrocardiogram was watched on an oscilloscope, so there is no way of accurately measuring the time intervals mentioned above However they were agreed upon by the several observers present It appeared that the whole period of arrhythmia did not last more than five minutes

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[1] Hill A. B. *Lancet* 1953 i 296
[2] Locke, R. A. J. Amer med Ass 1919 73, 759
[3] Urbach. Arch *Derm. Syph* Wien 1924 146 140

[4] Schultz, W *Klin Wschr* 1930 9 2193
[5] Foster C A., O'Mullane E. J Gaskell P Churchill Davidson H C. *Lancet* 1955 ii, 614

The diagnosis in this child was later confirmed at thoracotomy (Mr H R S Harley) and there were pulmonary infundibular and valvular stenoses At operation bradycardia was the only arrhythmia observed

I am not aware of ventricular fibrillation having been previously reported under catheter conditions in Fallot's tetralogy There has been some doubt as to how useful procaine amide would be in serious ventricular arrhythmia, but, while it is impossible to be sure about cause and effect in a case like this, on two occasions there was an improvement in the rhythm following the administration of the drug In the event of the drug being less effective it would be very difficult for a physician to decide just how early he must resort to thoracotomy and cardiac massage

We are not keen on trichloroethylene for anæsthesia in these circumstances and much prefer to supplement the bromethol with a little intravenous pethidine only In these small children, however, the veins do not always encourage the anæsthetist to adopt this method

At this hospital a number of children have now been catheterised in the first weeks of life and many in the first years This is the first untoward episode that has occurred during catheterisation, and it has been very gratifying to find how much helpful information can be gathered even in the very young

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Penarth Glamorgan

HUGH A FLEMING

## SODIUM AND POTASSIUM CONCENTRATIONS IN KWASHIORKOR

SIR,—Hansen and Brock have suggested[1] that electrolyte imbalance is important in the pathogenesis of nutritional œdema of the kwashiorkor type They reached this conclusion after observing that serum-potassium levels in infants with kwashiorkor "were significantly lower than normal on admission and rose with treatment" The serum sodium levels of the same children could not be correlated with degree of œdema or treatment

PLASMA CONCENTRATIONS OF SODIUM AND POTASSIUM BEFORE AND AFTER TREATMENT

| Case | Before treatment | | | After treatment | | |
|---|---|---|---|---|---|---|
| | Plasma-albumin (g per 100 ml ) | Sodium (m.eq per litre) | Potassium (m eq per litre) | Plasma albumin (g per 100 ml ) | Sodium (m eq per litre) | Potassium (m eq per litre) |
| 1 | 2 0 | | | 5 0 | 141 | 4 1 |
| 2 | 2 4 | 142 | 3 9 | | | |
| 3 | 1 3 | 142 | 5 0 | 3 9 | 144 | 4 4 |
| 4 | 1 9 | 143 | 4 3 | | 142 | 2 7 |
| 5 | 2 3 | | | 3 8 | 146 | 4 4 |
| 6 | 2 2 | 137 | 4 8 | 2 1 | 142 | 4 2 |
| 7 | 1 1 | 139 | 4 8 | | | |
| 8 | 1 6 | 149 | 4 7 | 5 1 | 140 | 4 4 |
| 9 | 0 9 | 140 | 3 7 | 2 0 | 140 | 4 9 |

In view of this report it may be of interest to record the serum potassium and serum sodium levels in a small series of children with kwashiorkor before and after treatment with high protein diet The investigations were made at the Mulago Hospital, Kampala, Uganda

*Methods*—Blood was obtained by puncture of the internal jugular vein, and was heparinised Sodium and potassium were estimated with an internal standard flame photometer Plasma albumin was determined by the biuret method

The table shows that the mean plasma-potassium concentration in seven children with severe œdema was 4 5 ± 0 1 (standard error) m eq per litre The mean value after treatment, when the plasma albumin had risen from 1 7 ± 0 1 to 3 4 ± 0 7 g per 100 ml and the infant had lost all or most of the visible œdema, was 4 2 ± 0·1 m eq per litre The mean plasma sodium concentration on admission was 141 7 ± 1 6 and after treatment 142 1 ± 1 3 m eq per litre We are unable to give potassium and sodium values for "normal" infants in Uganda since any child admitted to Mulago Hospital is likely to have been living on a protein deficient diet

Our results suggest that hypokalæmia is not an intrinsic feature of kwashiorkor A possible explanation of the difference between our findings and those of Hansen and Brock is that the infants whom we investigated had either no diarrhœa or diarrhœa which was very mild Perhaps the diarrhœa present in Hansen and Brock's patients was sufficiently severe to produce the potassium depletion which they found[2,3]

We should like to thank Mr K E Blackmore and Siste Joan Greaves for technical assistance We are indebted t the Colonial Medical Research Committee for financia support

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H HELLER
H SCHNIEDEN

## A LIVER POISON WITH UNUSUAL PROPERTIES

SIR,—In going through literature on porphyrins found a very interesting paper about jaundice, a pape which seems to me to open new ways for the experimental study of jaundice and bile secretion

In 1936, in a paper[4] on the disease geeldikkop in Sout African sheep, Quin presented some remarkable observation on the action of alcoholic extracts of the plant *Lippia rehmanni* (Pears) on the liver and bile secretion in sheep

Quin gave alcoholic extract of about 500 g of lippia to healthy young Merino sheep with bile fistula and a fair constant bile secretion amounting to about 150 ml of dar *green bile per 24 hours During the following 24 hours t* bile was remarkably reduced in volume and its colour striking changed After 24 hours it was clear sea green and aft 27 hours it was colourless The 24 hour output was reduc to about 40 ml During the third day the bile began regain colour, and after 8 or 9 days its colour was norm again Simultaneously jaundice of great intensity develope the serum was definitely yellow after 24 hours, and de brownish yellow after 48 hours, on the third day clinic jaundice was marked

The most remarkable feature of this poisoning, howev was that the liver showed no pathological alterations importance, even on microscopical examination No obstr tion of the bile ducts was found There were no signs hæmolysis, the Hb level and red cell count were stable a no hæmoglobin was found in the plasma

This seems to be a poison which is capable of produc severe jaundice without hepatocellular damage obstruction of the bile passages, and which gives rise secretion of white bile And its actions are large "functional" and reversible

It is surprising that the action of this poison has n yet been used experimentally—e g, in dogs or ra There are many problems in the physiology and path logy of bile secretion and jaundice (summarised in recent monograph[5]) which could be studied in this wa

I want to point out specially that Quin's findin seem to support the hypothesis of lymphogenous jaund due to secretion from the blood via the liver cells to t lymph instead of to the bile[6] It would be a very ea and elegant explanation of the action of lippia to s that it simply reversed the secretion from the bile to t lymph

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[1] Hansen, J D L, Brock J F *Lancet* 1954 ii, 477 Brock, J F Proceedings of 3rd International Congress of Nutrition Amsterdam, 1954

[2] Gamble, J L Chemical Anatomy Physiology and Patholo of Extracellular Fluid Cambridge Mass, 1947

[3] Newburgh L H Significance of the Body Fluid in Clini Medicine Springfield, Ill 1950

[4] Quin J I *Onderstepoort J vet Sci* 1936, 7, 351

[5] With T K. Biology of Bile Pigments Copenhagen 1954

[6] With, T K *Acta med scand* 1947 128 25 *Ibid* 1949 sup no 234 p 331 See also Liver Disease Ciba Foundati Symposium London, 1951, p 202

Further, the action of lippia is a strong argument against the hypothesis that the direct diazo reaction (Hijmans van den Bergh's direct reaction) is peculiar to bilirubin which has passed the liver cells. For the jaundiced plasma in the lippia-poisoned sheep gave a strong direct diazo reaction although it did not pass into the bile.

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TORBEN K. WITH.

## MEDIAN-NERVE PALSY FOLLOWING BEE-STINGS

SIR,—The report of Mr. Bailey and Mr. Bolton Carter (March 12) on two cases of median-nerve palsy complicating hand infections reminded me of a personal experience of median-nerve palsy resulting from bee-stings.

Last summer, when manipulating a vicious stock of bees, I was stung badly on the front of both wrists—parts of the body singularly attractive to bees. The attack was concentrated and localised. There were few stings on the fingers (because they were smeared with dimethyl phthalate) and none above the wrists (I was wearing elastic cuffs). There was little visible swelling, but I was kept awake that night by intense tingling in the thumb and in the index and middle fingers. Next day the fingers were flexed and any attempt to straighten them actively or passively was very painful. The little finger was normal. About 48 hours later, while I was still wondering what had happened, the symptoms began to subside rapidly.

I looked upon it as an acute carpal-tunnel syndrome, and the cases reported last week support the idea that the median nerve was involved in deep-seated œdema resulting from the stings.

Chase Farm Hospital,
Enfield, Middlesex.

C. ALLAN BIRCH.

## INFECTION WITH CRYPTOCOCCUS NEOFORMANS

SIR,—The report last week of two cases of cryptococcosis by Dr. Beck and his colleagues raises interesting problems.

They state that case 1 was originally diagnosed as Hodgkin's disease by cervical lymph-node biopsy, but that the development of a terminal cryptococcal meningitis revealed the true nature of the disease. They thus imply that the Hodgkin's lesions arose as a result of cryptococcal infection. Yet the lesions described were typical of Hodgkin's disease in their microscopical appearance and showed no cryptococci, while the histology of the meningitis, where cryptococci were abundant, was that of chronic inflammation. It is difficult to accept that an organism can produce an inflammatory reaction of the meninges at the same time as a Hodgkin's-like picture elsewhere. It would seem more likely that this infection arose as a terminal event in the course of typical Hodgkin's disease. This view is supported by the fact that the lymph-node enlargement preceded the cryptococcal meningitis clinically, and at necropsy the Hodgkin's lesions were extensive while the meningeal inflammatory infiltrate was sparse.

The explanation for the association between these two diseases may be connected with the breakdown of certain immunity mechanisms that is known to occur in Hodgkin's disease. It was discovered many years ago that the proportion of tuberculin-positive reactors is much lower in Hodgkin's disease than in the general population,[1] and Dubin[2] has shown that the incidence of Wassermann positivity in Negro patients with Hodgkin's disease is significantly lower than in the Negro population in general. It is possible that natural antibodies giving resistance to cryptococcal infection in healthy people are absent or reduced in cases of Hodgkin's disease.

Both the patients described by Dr. Beck and his colleagues had heavy doses of antibiotics. Direct stimulation of fungal growth by antibiotics has been shown to take place in the case of *Monilia albicans*,[3] but so far no work has been published in this connection with regard to torulosis.

Case 1 was given intrathecal penicillin and streptomycin as well as these antibiotics systemically and sulphonamides orally. The patient's condition deteriorated rapidly, and he died after a week of this treatment.

Eighteen months ago I saw in this hospital a case in which the cryptococcosis presented as a terminal septicæmia, with no focal lesions, in a patient with advanced Hodgkin's disease.[4] The patient had been treated with large quantities of sulphonamides, penicillin, streptomycin, and chloramphenicol during the three months before death. Here too it was possible that stimulation of cryptococcal growth by these antibiotics might have been the cause of the unusually acute infection.

May I therefore suggest that until exact knowledge is obtained on this point it would be as well to withhold local and systemic antibiotics in the treatment of torulosis unless laboratory tests have shown that the cryptococcus is sensitive to any particular antibiotic.

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I. MICHAELS
Registrar in Pathology.

## B.C.G. VACCINATION

SIR,—Dr. Webster (March 5) hits the nail on the head when he says that "the fundamental question to which we do not know the answer is whether a positive skin reaction is really very important in immunity to tuberculosis."

A positive skin reaction is a measure of hypersensitivity and not of immunity, though of course immunity and hypersensitivity may be related. Brownlee[5] has emphasised that the characteristic widespread tissue destruction of tuberculosis follows the conditioned hypersensitivity. Hypersensitivity without immunity is clearly undesirable.

We know that a negative skin reaction can often be converted into a positive one by infection with tubercle bacilli, B.C.G., or other related organisms. We also know that a positive reactor can be converted into a negative one by desensitisation with either old tuberculin or purified protein derivative. But we do not know whether there is any difference between the negative reactor who has never been positive and the negative reactor who went through a positive phase and became negative as a result of therapeutic or natural desensitisation. If we accept Godlowski's[6] enzymatic concept of allergy, the distinction between these two types of negative reactor is clear cut. The negative reactor who has never been through a positive phase has tissues which are insensitive to the particular antigen of the tubercle bacillus which causes hypersensitivity. The negative reactor who has been positive and has become negative through desensitisation produces sufficient antibody to destroy the antigen before it can reach the interior of the sensitised cells.

Godlowski's hypothesis also explains why in some cases of sarcoidosis the reaction cannot be converted from negative to positive with B.C.G. Such patients are negative reactors because they have been desensitised naturally, and although their tissues are still sensitive to antigen they do not exhibit hypersensitivity because the antigen is neutralised by antibody before it can do its destructive work.

Professor Heaf (Feb. 12) points out that the evidence is that B.C.G. vaccination does offer considerable protection against the development of primary tuberculosis but exerts little control over the development of postprimary lesions. Whether primary or postprimary tuberculosis is the more lethal or crippling disease in this age of chemotherapy is undecided. But the wisdom of protecting the population against primary tuberculosis and leaving it susceptible to postprimary tuberculosis is doubtful. As Professor Heaf so rightly says, "Perhaps the greatest disadvantage associated with B.C.G. vaccination is the unwarranted confidence that it has inspired in laymen in many countries."

It would seem that what is required is a vaccine which will confer immunity and will at the same time desensitise the patient. When we are satisfied that B.C.G. does confer some degree of immunity, subsequent desensitisation could be secured with old tuberculin , but at present this is clearly not practical on a large scale

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[1] Reed, D. M. *Johns Hopk. Hosp. Rep.* 1902, 10, 133.
[2] Dubin, I. N. *Ann. intern. Med.* 1947, 27, 898.
[3] Tear, C. C., Winter, W. O. *J. infect. Dis.* 1949, 85, 268.

[4] Levene, M., Michaels, L. *J. clin. Path.* (in the press).
[5] Brownlee, G. *Irish J. med. Sci.* October 1951, p. 463.
[6] Godlowski, Z. Z. Enzymatic Concept of Anaphylaxis and Allergy. Edinburgh, 1953.

We can measure hypersensitivity by the skin reaction in a single human being, but we have as yet no ethical method of measuring individual immunity , consequently we have to rely on cumbersome statistical estimates of immunity, and we should therefore not confuse ourselves by thinking that immunity and hypersensitivity must have something in common

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Sussex
G E LOXTON

## TUBERCULOSIS IN IMMIGRANTS

SIR,—In his letter of Jan 29 Dr James says that " in populations with high tuberculosis death rates there is always a high proportion of positive reactors, and a high reactor-rate in children is always associated with a high death-rate in young adults " The data as found in Lewis do not bear this out

In Lewis there is the town of Stornoway (population 4817) and four rural parishes—Stornoway (7842), Barvas (5019), Lochs (3111), and Uig (2716) The villages comprising the parish of Stornoway are situated on either side of Broad Bay at distances of from $2^1/_2$ to 14 miles, while all the other parish villages are at least 12 to 35 miles from the town The more remote the lower the positive reactor rate but the higher the death rate (see accompanying table)

TUBERCULOSIS IN LEWIS

| — | Stornoway burgh | Stornoway parish | Barvas parish | Lochs parish | Uig parish |
|---|---|---|---|---|---|
| Population | 4817 | 7842 | 5019 | 3111 | 2716 |
| % positive in 1949<br>5–6 year (entrants) 1954 | 24<br>4 5 | 24<br>6 9 | 18 | 11<br>2 2 | 12 |
| % positive in 1949<br>5–12 year 1954 | 50<br>25 | 25<br>17 | 20<br>10 | 20<br>11 | 15<br>7 |
| *Tuberculosis deaths* | | | | | |
| 1945–50 | 23 | 79 | 33 | 27 | 23 |
| 1949–54 | 12 | 33 | 19 | 17 | 10 |
| Sputum - positive cases (1945–54) | 29(a)<br>16(d)<br>45(t) | 82(a)<br>30(d)<br>112(t) | 36(a)<br>14(d)<br>50(t) | 18(a)<br>11(d)<br>29(t) | 16(a)<br>4(d)<br>20(t) |

a = alive, d = dead, t = total

*The 5–12 age-group was chosen for comparative purposes because* after the age of 12 the country children come to the Nicolson Institute in the burgh of Stornoway

Stornoway, Lewis
R STEVENSON DOIG

## CHEMOTHERAPY OF LEPROSY

SIR,—My experience in Northern Rhodesia prompts me to endorse Dr Jopling's remarks (Jan 8) In 1951 I saw something of Dr Lowe's outstanding work in Eastern Nigeria and was greatly impressed, but results of treatment here in Rhodesia have not been equal to Dr Lowe's

Since 1950 some 1006 patients here have had sulphone treatment, and while results on the whole are good there is a " hard core " of cases which show little response It is difficult to assess results accurately in terms of statistics, as conditions here are primitive and patients frequently abscond during treatment , but of the initial group of 52 patients we started on diaminodiphenylsulphone (D D S ) in 1950, 5, all with severe lepromas, have died, while 20 are still here under our care For five years these 20 patients have been under close medical supervision and on continuous D D S , and 7 of them still show masses of bacilli in their smears with no material change in their clinical condition 10 lepromatous patients that showed a few bacilli in smears in 1950 have now become persistently negative and the disease appears to be arrested 3 patients were tuberculoid cases, bacteriologically negative when treatment was commenced

These results do not encourage complacency Much leprosy is self limiting and it is the " hard core " of resistant and contagious cases we must attack if the disease is to be wiped out It will be a pity if the mass use of sulphones diverts attention from the need for more effective remedies

Chitokoloki Leprosy Settlement,
Balovale,
Northern Rhodesia
J T WORSFOLD

## ADRENALECTOMY FOR HYPERTENSION

SIR,—This title of your leading article on Jan 8, the statement in it that " hypertension is not associated with increased secretion of " and the quotation from Jeffers et al —" This is an experimental approach which cannot at present be recommended as a treatment for hypertension "—all suggest that hypertension is an entity which will respond to a single therapeutic procedure

This attitude is anachronistic It is a " fossil fancy of a bygone age " when clinicians believed that a single mechanism was responsible for the elevation of the blood-pressure Today we know that hypertension may be brought about by six or seven distinct mechanisms, each of which must be dealt with differently To refer to the treatment of hypertension in this way is as unjustifiable as to talk about the treatment of pyrexia or of an increased erythrocyte sedimentation rate

We are all guilty of this solecism, and one reason may be our realisation that the majority of cases of hypertension fall into the group labelled " essential," where it is likely that a single mechanism is responsible for the increase of the blood pressure

I presume that this thought lay behind your confident assertion " There is now good evidence that, except in phæochromocytoma, hypertension is not associated with increased secretion of adrenaline or noradrenaline, and it is the adrenal cortex that plays the more important part in pathogenesis " I find it difficult to accept this view, for I believe that the adrenal cortex has little or nothing to do with the pathogenesis of essential hypertension On the other hand, I regard the evidence in favour of noradrenaline as particularly strong [1] Here I would only emphasise that the fall in blood-pressure which follows destruction and blocking of the sympathetic pathways is best explained by these procedures interfering with the production and/or the secretion of noradrenaline

That the adrenal cortex plays little or no part in the pathogenesis of essential hypertension is indicated by these facts

1 Cushing's syndrome (adrenal cortical hyperplasia, adrenal cortical adenoma) is rare

2 Essential hypertension is common

3 The stigmata of Cushing's syndrome are not found in essential hypertension

4 The cause of the hypertension in Cushing's syndrome is almost certainly plethora induced by sodium retention

5 Sodium retention is not a feature of uncomplicated essential hypertension

6 Goldzicher [2] states " Injection of cortical extracts although raising the blood pressure in adrenal insufficiency, does not alter the blood pressure in normal controls There is no reason to believe that cortical hormone is directly responsible for an increase in the arterial tonus, for the re establishment of the normal blood volume explains the reaction of the adrenalectomised animal "

7 McMichael [3] states ' efforts to demonstrate increased excretion of suprarenal cortical substances in the urine of hypertensives " [presumably essential hypertensives] " have not yet succeeded "

Goldblatt's observation that hypertension induced experimentally by constriction of one renal artery could be abolished by adrenalectomy has little bearing on the solution of our problem All it proves is that hypertension produced by one mechanism (renal hypertension) can

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1 Menof P *Lancet*, 1954, ii 996 *Ibid* Jan 22 1955, p 204
2 Goldzicher, M A The Endocrine Glands New York 1939
3 McMichael, J *Brit med J* 1952 i, 933

be neutralised by hypotension induced by another (in fact by two others—namely, the mechanisms responsible for the sodium depletion and noradrenaline deficiency)

The fact that hypertension following bilateral nephrectomy is abolished by bilateral adrenalectomy can be explained in much the same way, but whether such findings demand an explanation is open to doubt The physiological insult in these experiments is so great that one wonders whether the results might not admit of more than one interpretation For example the mechanism responsible for renoprival hypertension might well be quite different from that behind renal hypertension in which event conclusions based on the identity of the two mechanisms would be invalid

Johannesburg PERICLES MENOF

## AFTER THE ACCIDENT

SIR,—May I support Mr Gissane s timely remarks last week and his emphasis on the need for better organisation and facilities for the treatment of the injured If there existed sufficient adequately staffed and equipped accident services to deal efficiently and quickly with the constant stream of accidents of all kinds they would not only reduce the enormous cost of these accidents to the nation but would provide the pool of staff of all grades accustomed to dealing with the injured, which is the only sound foundation on which to base plans for dealing with major accidents

The treatment of the injured makes heavy and continuous demands on all concerned and gives satisfaction only when it is carried out under proper conditions This applies both *to patients and to staff* In planning equipping and staffing accident services both these factors should be taken into account A strong stimulus to the maintenance of a highly skilled staff in this important field would be the opportunity for them to give a prompt and complete service to all the patients We are fortunate in Oxford in having an accident service planned on this basis though the needs have already to some extent outstripped the provisions made for them

J C SCOTT
Director Accident Service
United Oxford Hospitals

## FEAR AND APPENDICITIS

SIR,—Doctors in general practice in Nairobi very seldom see cases of appendicitis among the Negro population My father who practised in Nairobi for over fifty years saw less than half a dozen cases in that time In my own practice which is of considerable size I saw no cases at all for eight years then in 1953 I had 4 within a few weeks The Mau Mau terror was then at its height and all 4 patients were living under great strain anxiety, and fear

CASE 1—A Negro woman of 22 was married to a European The couple were well known and the husband was in bad odour with the government because of his politics Life was hard and precarious. The woman was brought to me complaining of pain in the right iliac fossa She was very distressed, and said that the Mau Mau were threatening her life because she was married to a European Her temperature was 100 4 F She was tender in the right iliac fossa particularly over McBurney s point No other focus of infection was found and there was nothing relevant to appendicitis in her previous history She refused to go to hospital so I treated her with penicillin and streptomycin by injection and aureomycin by mouth. She made a rapid and uneventful recovery

CASE 2—A Negro woman married to a European farmer whose life had been threatened by the terrorists complained of intense pain in the right iliac fossa She had vomited several times. Her temperature was 99 7 F and she was very tender in the right iliac fossa, with pain radiating to the right leg There was nothing relevant in her history and no other focus of infection was found She refused t go to hospital and so was treated conservatively in the same way as case 1 She recovered from this attack within a fortnight ; later when her symptoms returned appendicectomy was successfully performed

CASE 3—A Negro woman the wife of a government employed Negro whose life had been threatened by the terrorists complained of pain in the right iliac fossa of one month s duration She looked thin and ill Her temperature was normal but a lump the size of a hen s egg was palpable in the right iliac fossa There was no other focus of infection and there was nothing relevant in her history She was persuaded to go to hospital where she was operated upon and made an uneventful recovery

CASE 4—A Negro woman living with a European farmer complained of intense pain in the right iliac fossa since the previous day Three attempts had been made on the life of her husband and there had been much theft and attempted arson on the farm as well as malicious damage The woman was intensely harassed by these events and afraid for the safety of her husband and children. She was extremely tender in the right iliac fossa Her temperature was 101 2 F She was tender on pelvic examination and flexing the right leg caused pain She refused operation so I treated her conservatively and she recovered in twenty days. Subsequently her symptoms returned and this time she agreed to operation, which proved successful

In none of these cases was any focus of infection discovered All 4 patients were taking their normal African diet Extreme anxiety, worry, and fear were present in all, and I believe they precipitated the illness That anxiety, worry and fear may contribute to appendicitis has been debated for many years I saw a few cases in England, during the late war, in which mental factors were considered to be of importance

Nairobi Kenya AYRES L RIBEIRO

## HOSPITAL STAFFS

SIR—In view of the severely restricted number of consultant vacancies which are likely to arise, and to give senior registrars a more reasonable prospect of established posts with corresponding security of tenure, may I suggest the following

1 That an additional grade of senior registrar (F) be introduced this new grade to have a maximum salary of £200 more than the existing grade and to be regarded as holding established posts with permanent status

2 That boards of governors and regional boards be empowered to confer (F) status on selected senior registrars selection being based on recommendations from consultants at a yearly review of senior registrars

3 That boards be authorised to increase their existing establishments of senior registrars by an additional number of senior registrars (F) these additional posts to be at the disposal of boards for duties throughout the region The number of additional posts should be related to the total absences by way of annual leave sickness &c, during the twelve months prior to the yearly review

I feel that such action would enable something to be done for the really worthy senior registrar More important, it would give them and their families the security which they have a right to expect after many years in junior appointments

Whittington Hospital
Archway Wing London N 19

D J McCARTHY
*Hospital Secretary*

## ARTIFICIAL HIBERNATION IN POLIOMYELITIS

SIR—Dr Ritchie Russell (Feb 26) strongly opposes the use of artificial hibernation in the acute stage of poliomyelitis Dr Russell states that ' this is not a situation in which experiments on patients with new drugs is justifiable ' We agree that all possible work animals should be completed before new methods tested on man But in the case of artificial
a great number of experiments have been
furthermore the method has been subje
trials for more than three years in sev
diseases—for instance meningitis cu ,
and tetanus

In the case we described (Feb 19, p 409) we found a desperate situation which could not be dealt with by conservative means This case is to be reported in detail in the near future We still think that in such circumstances it is justifiable to use a new method which is believed to be reasonably safe

Allmänna Sjukhuset
Malmö, Sweden

KNUT HALGER
GUNNAR MIORNER

## MONGOLISM IN AFRICANS

SIR,—There appears to be a widespread feeling amongst psychiatrists—e g, Carothers, Tooth, and Tredgold—that mongolism does not occur among Africans We were therefore interested to read the letter in your issue of Oct 23 by Dr Jelliffe, stating that he did not meet a single case in his long experience of pædiatrics in Nigeria He adds his view that mongolism among Negroes in America is due to the admixture of Caucasian strains

His letter prompts us to mention our experience in Kampala, Uganda, where within the last three months we have seen six undoubted cases of mongolism among the local indigenous tribes (Baganda and Lango), where the possibility of any admixture of non Negro strains can be discounted We hope to describe these cases more fully in the near future

Mulago Hospital
Kampala, Uganda

J LUDER
L K MUSOKE

## A NON-PULSATILE AORTIC ANEURYSM

SIR,—It is usually accepted that aortic aneurysm can be diagnosed on combined clinical and radiographic examination The following case, however, was sufficiently atypical to constitute a real diagnostic problem

An unmarried woman of 55 was admitted to this hospital with nine months' history, dating from a right sided pleurisy, of dragging pain in the right loin, radiating to the right shoulder, lumbar spine, mid abdomen, and groin At first the pain was intermittent, but latterly it became continuous even when she lay down, and sudden movement made it worse The pain was not related to meals, but she had lost about two stone in weight and complained of mild dysphagia There was some frequency of micturition, but no dysuria She denied any significant previous illness

Apart from moderate hypertension (172/92 mm Hg) and mild anæmia, the only definite abnormality found on routine clinical examination was a palpable right kidney Examination of the central nervous system was quite negative

Intravenous pyelography was negative, but X ray examination of the chest showed generalised cardiac enlargement with a large soft tissue paravertebral shadow, not sharply demarcated, in the mid thoracic area, there was erosion of the bodies of the eighth and ninth thoracic vertebræ, but no diminution of the disc spaces Barium swallow showed the œsophagus to be partially compressed, just above the tracheal bifurcation Tomography revealed a "glandular mass" in the posterior mediastinum and careful X ray screening showed no expansile or transmitted pulsation in this mass

Blood Wassermann and Kahn tests were reported as negative The plasma protein ratio was just inverted, and blood films showed a mature polymorph leucocytosis (11,000 to 16,000 per c mm) The erythrocyte sedimentation rate varied between 45 and 55 mm in the first hour Sternal marrow showed slight eosinophilia, but no evidence of myelomatosis There were no enlarged superficial lymph nodes available for biposy

A tentative diagnosis of spinal tuberculosis with a paravertebral abscess was made after further consideration of the X-ray appearances, although admittedly these were not typical A Mantoux test (1 in 1000) was positive, but no tubercle bacilli were found on smear or subsequent culture of three gastric aspirates There was no evidence of wasting, either before or during her stay in hospital

Six weeks after admission the patient suddenly vomited two pints of bright red blood Following sedation, a three pint blood transfusion and continuous intravenous fluids were given, and during the next few days she improved sufficiently to begin small feeds However, on the eighth day she had a further massive hæmatemesis and died within a few minutes

*Necropsy* revealed a large fusiform aneurysm of the descend thoracic aorta, with a fistula between the sac and the œsophagus, about one inch in diameter The sac was thickly lined with laminated thrombus Sections of the aortic wall at various levels showed changes characteristic of syphilitic mesaortitis, still in an active phase The aneurysm had eroded deeply into the bodies of the eighth and ninth thoracic vertebræ Both kidneys were unduly mobile and a small retention cyst was found in the right kidney Specimen of blood taken at necropsy again gave a negative W R.

It is difficult to see what measure (short of thoracotomy) would have led to a correct ante mortem diagnosis The first hæmatemesis occurred twenty four hours before proposed œsophagoscopy, which would probably have been fatal in itself The absence of wasting was evidence, not fully appreciated, against a reticulosis, chronic tuberculosis, or pyogenic disease The negative W R might have been viewed with more suspicion had we known before the patient's death of her three children by different fathers

The recovery from her first hæmatemesis was strongly against its being the result of an aneurysm a sudden aneurysmal rupture is usually fatal within minutes—as on the second occasion But at necropsy no other healed aneurysmal rupture, œsophageal varices, or primary gastric lesion was found, and the second rupture was almost certainly at the same site as the first Partially organised intra aneurysmal thrombosis may have sealed the gap temporarily, in the patient's suddenly hypotensive state, and this may also have been the explanation of the atypical radiological findings

*I wish to thank Dr J W Buchanan,* consultant physician to the East Fife Group of Hospitals, for permission to publish this case and for his advice and criticism, Dr Peter Aitken for permission to use the radiological reports, Dr L Grant Leitch for the necropsy details, and the other consultants who advised on this case for their help

Victoria Hospital,
Kirkcaldy, Fife

GILBERT R BRACKENRIDGE

## A BARBITURATE ANTAGONIST

SIR,—Following Dr Harris's account (Jan 22) of the action of β, β-methyl ethyl glutarimide (NP 13) we report what we believe to be the first recorded instance in Britain of this drug's employment against severe barbiturate poisoning

The patient, a man aged 25, had taken gr 30 each of quinal barbitone and amylobarbitone in a combined preparation at 2 50 P M on Feb 27 He had been drinking heavily the previous day On arrival at Whittington Hospital at 6 P M he was in deep coma His respiratory rate was 16 per minute, and there was generalised depression of all reflexes, with complete absence of pupillary, corneal, knee, and plantar reflexes After conventional treatment the light reflex returned by 11 P M, but serious deterioration set in at 3 45 A M on the following day with the development of right basal pneumonia

Through the kindness of Dr A E Alcock, of Nichola Products Laboratories Ltd, we obtained a supply of NP 13 together with 2 4 diamino 5 phenylthiazole ('Daptazole') and the combined treatment as suggested by Prof F H Shaw was started at 2 15 P M on Feb 28, nearly twenty four hours after the *barbiturates had been taken* The *initial* dosage was daptazole 15 mg and NP 13 50 mg given at three minute intervals into the delivery tube of an intravenous set containing tetracycline

At the beginning of treatment the corneal, knee, and plantar reflexes were still absent The pulse rate was 11 and respiration rate 30 per minute After thirty minutes the knee jerks returned and respirations became deeper, and fifteen minutes later a normal plantar reflex appeared At the end of two hours all tendon reflexes and a weak cough reflex were present, but the patient was still considered to be in danger Fresh supplies of the drugs were obtained, and, as there appeared to be no risk of overdosage, double quantities were given at the same time intervals from 7 30 P M After two injections a withdrawal reflex was obtained, the patient coughed strongly, and the corneal reflex returned Three further double injections were given, making a total of NP 13 2 g and daptazole 600 mg An uneventful recovery followed

Two conclusions may be permissible from this single case First, this combination of drugs is effective in once barbiturate poisoning and secondly, the intermittent method of administration provides a wide margin of safety

Whittington Hospital,
Archway Wing
London N.19

E MONTUSCHI
P D WICKENDEN

## HORROR COMICS

SIR,—May I express my appreciation of your leading article of March 5 Your enlightened and comprehensive statement is in contrast to what has happened in the United States

Here no one single medical journal has taken up this specific problem and not one psychiatric journal has so much as mentioned the public health aspect As a matter of fact one of the crime-comic book publishers was permitted by a popular medical journal to justify his position in an article In Defence of Comic Books—which is like permitting a distiller to write In Defence of Alcoholism

You deserve the gratitude of parents for having treated the comic book problem as a public health problem. Public health as William Welch Sudhoff and Henry Sigerist often pointed out is international And just as the current debate in the British House of Commons could well be a model for the United States Congress which has now twice brushed off the comic book problem so *The Lancet* may well be a preceptor for our American medical journals

New York

FREDRIC WERTHAM

## COSMETICS

Mr Ralph G Harry F R I C., writes

I am at present revising my book *Cosmetic Materials* and am anxious to obtain as much information as possible on primary irritation or sensitisation arising from substances used in the cosmetic, toilet and pharmaceutical industries. I should be very glad to receive brief details of instances in which the offending ingredients have been definitely confirmed by skin tests If any of your readers would be good enough to supply such detail I should be very grateful if they would write to me at 60 Broad Walk, Heston, Middlesex.

# Medicine and the Law

## Broken Needle in Child's Throat

A CHILD of 10 was undergoing tonsillectomy and adenoidectomy when the right tonsillar bed began to bleed severely While the surgeon was attempting to control the bleeding by stitching the anterior and posterior faucial pillars together the needle broke and two-thirds of it (about $^1/_2$ in ) remained in the child's throat. A stitch was inserted with a fresh needle and the bleeding brought under control. At that point the light in the surgeon's headlamp failed, plunging the theatre into darkness The bulb was quickly replaced, and the surgeon began a search for the broken needle which continued unsuccessfully for an hour The needle was later removed in another hospital by means of an electromagnet

Subsequently the child's father on his daughter's behalf, claimed £5000 damages from the surgeon Giving judgment in the Edinburgh Court of Session on March 4 Lord Guthrie said that examination by a specialist revealed heavy scarring and immobility of the soft palate Despite speech therapy the girl's speech was difficult to understand It was possible that this might improve but her voice would not be adequate for singing He held that if the surgeon had exercised reasonable care and skill he would have desisted from his blind search It should have occurred to him that prolonged probing and stitching of the fibres would have serious and possibly permanent consequences. £850 damages were awarded against the surgeon.[1]

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[1] Times, March 5, 1955 *Glasgow Herald*, March 5, 1955.

# Parliament

## QUESTION TIME

### Diagnosis of Pneumoconiosis

Replying to a question, Mr OSBERT PEAKE Minister of Pensions and National Insurance said that he did not think an inquiry into the causes of the wide variation in the proportion of pneumoconiosis claims diagnosed as such by the pneumoconiosis medical panels in the different areas would serve any useful purpose

Mr W N WARBEY Is the Minister aware that the wide variation in diagnosis from as high as 75% in Scotland and 70% in the West Midlands to as low as 47% in the East Midlands is causing a great deal of uneasiness in the coal mining industry Now that the scheme has been working for some years, does the Minister not think it would be a good thing to have an inquiry both into the diagnostic criteria and into the question of whether it is a really good thing to have a panel of medical experts functioning as a final appeal tribunal for benefit claims? Mr PEAKE I cannot accept that the proportion of successful claims in different districts shows that there is any wide variation in diagnosis in those districts. The fact is that the condition giving rise to the disease the form of the disease itself, and the awareness of the risk of disease vary greatly from district to district

### *Deaths from Gas Poisoning*

Replying to a question, Mr GEOFFREY LLOYD Minister of Fuel and Power said that he shared the public anxiety regarding the increasing number of cases of gas poisoning in this country It was unfortunately an unexpectedly complicated problem because the idea that it was simply the old gas mains which caused this trouble was not borne out by the facts. Quite new gas mains in perfect condition had caused trouble in severe weather That was why a special engineering investigation was being made This was particularly a problem of older people and the Ministry were in touch with the old people's organisations with regard to it

### Mercury Poisoning and Pink Disease

Replying to a question Mr IAIN MACLEOD Minister of Health said that he was advised that the degree of association between mercury poisoning and pink disease had not been clearly established. Many cases of pink disease had no demonstrable association with ingestion of mercury and the great majority of children who had been given mercurial preparations showed no sign of the disease It seemed possible that some few infants might have an exceptional sensitivity to mercury In 1952 and 1953 64 children under five years old were certified as having died from pink disease and 4 from mercury poisoning in 2 cases both pink disease and mercury poisoning were mentioned in the death certificate

### Radioactive Substances

Mr FREDERICK WILLEY asked the Minister of Labour how many members of H.M. inspectorate of factories were specially qualified to deal with the effect of the use of radioactive substances —Mr HAROLD WATKINSON replied Six officers at headquarters with appropriate qualifications and experience have made a special study of the problem from the medical scientific and technical angle and the chief inspector of factories draws freely upon the expert advice of members of the radiological advisory panel of the statutory advisory committee appointed under the Radioactive Substances Act 1948 of the radiological protection service of the Medical Research Council, and of the Atomic Energy Authority itself Instruction has been given to all inspectors in the precautionary methods to be adopted in the use of radioactive substances.

### Medical Standards in the R.A.F

Mr GEOFFREY DE FREITAS asked the Under-Secretary of State for Air what changes there had been in the last two years in the medical standards for regular commissions in the general duties branch of the Royal Air Force —Mr GEORGE WARD replied Standards of visual acuity have been slightly raised and the standard of colour perception slightly

### Psychiatric Social Workers in

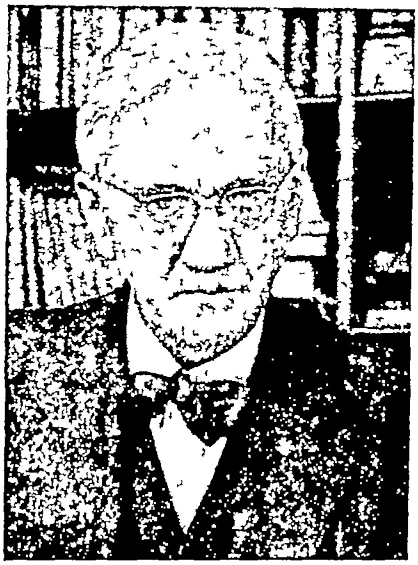
Replying to questions Mr JAMES STUART
State for Scotland said that psychiatric
employed at 11 of the 34 mental hospitals in
sion of aftercare for mental cases was
most part by the Scottish Association for
its local branches In 1953–54 contri
the association were made by 41 of the
ties comprising the councils of 22 com

# Obituary

## ALEXANDER FLEMING

Kt, M.B Lond , F R C.P , F R C S , F R S

> "While working with staphylococcus variants a number of culture plates were set aside on the laboratory bench and examined from time to time In the examinations these plates were necessarily exposed to the air and they became contaminated with various micro organisms It was noticed that around a large colony of a contaminating mould the staphylococcus colonies became transparent and were obviously undergoing lysis"



[ Life International

IN these matter-of-fact words Fleming announced the discovery of penicillin in 1929 It has sometimes been suggested that his observation was mere luck, and that he was unaware of the momentous possibilities of the substance which had fallen into his hands But this suggestion is mistaken Fleming himself agreed that he enjoyed good fortune in his discovery, but he had long been on the lookout for just such a substance as penicillin proved to be He did not delay in testing whether it was harmful to leucocytes, and he organised trials of its efficacy as a dressing for surface wounds twelve years before other investigators were able to prepare the substance in stable form and in sufficient quantity for its use as we know it today After 1940, as a result of brilliant work and great determination at Oxford, penicillin became a miracle drug, but Fleming could still justly say "It was bound to happen sometime" He may have thought regretfully that he might have pursued the problem further in the years immediately after 1928, but his conclusion always was "I was no chemist" It was essentially as a naturalist that he regarded himself, and his approach to bacteriology proved the accuracy of this self-assessment He took pleasure in the great variety of ways in which life was revealed in bacteria The beautiful, the curious, and the unexpected held an attraction for him, and this attitude sharpened his observation It would not be true to say that he was without preconceived ideas, but it could be said that his natural curiosity would always be stronger than any hypothesis that might be in his mind at the outset of a piece of work It could also be said that some of his preconceived ideas fully justified themselves—the faith in "natural antiseptics," for example, which led him as early as 1914–18 to put forward the proposition that the chemical laboratory might be neither the best nor the only place in which to seek for substances that could destroy bacteria without unduly disturbing the tissues and natural defences of the body As befitted a born naturalist, he was a master of bench work and laboratory methods of all kinds, and he took real pleasure in demonstrating the elegance of his methods for measuring the amount of penicillin in the blood—nearly as much pleasure, it often seemed, as he took in discovering penicillin itself It was characteristic of him that, when he realised that he could not at once use penicillin for treatment, he successfully exploited its possibilities as a technical aid in the isolation of hæmophilus organisms Interestingly enough, only a few months ago, he admitted that he rated his discovery of lysozyme as of greater potential significance than that of penicillin

Fleming sometimes spoke of a conviction that he was divinely guided in his great discovery, and this attitude did not commend itself to all his fellow scientists But natural curiosity and sincere piety are not incompatible qualities To a man of Fleming's time, brought up in the atmosphere of rural Scotland at the end of the 19th century, it was as natural and inevitable to say that a great and beneficial discovery like penicillin could not have been made by himself alone as it was to say grace before meat

He was born at Darvel in 1881, one of the seven children of an Ayrshire farmer He went to the village school and later to Kilmarnock Academy, but he was still only a lad of 13 when he came to London to join his brother, who was a doctor in practice in Marylebone After a couple of years at the Polytechnic Institute in Regent Street, he took a junior post in a shipping firm, joined the London Scottish, and was soon a crack shot as well as a first-rate swimmer Later he used to recall how on a hot summer day the London Scottish in their kilts outmarched some famous regiments on the way to Bisley and won the inter regimental shooting competition

Four years later a small legacy made it possible for him to make a fresh start, and on his brother's advice he decided to study medicine He went back to his elementary studies, passed the London Matriculation examination, and gained the senior natural science entrance scholarship at St Mary's Hospital medical school (It was said that he chose St Mary's because it then had a specially fine swimming team ) From that time his innate ability showed itself He won almost all the scholarships and prizes, and in 1908 he took honours in half a dozen subjects in the M B examination and won the university gold medal A year later he took the F R C S "in his stride"

It was a happy coincidence that Almroth Wright should have been developing his bacteriological researches at St Mary's at the very time that Fleming was seeking for an opening After qualification he entered Wright's laboratories, and soon, by his skilful technique, his accurate observation, and his tremendous zest for work, won a secure place in the remarkable team then working there D W C-J recalls them one by one

"Almroth Wright himself, the man of theory and its practical application , Stewart Douglas perhaps the leader in technical ingenuity and manipulative skill , John Freeman, who demonstrated the phenomenon of autoinoculation by variations in the opsonic index, who first made and used a pertussis vaccine , Leonard Noon, with whom he devised methods for the diagnosis and treatment of hay fever by means of pollens , John Wells, who died prematurely from a laboratory infection with glanders , John Matthews, very successful on the therapeutic side , William Parry Morgan who first induced *partial* pneumothorax in the treatment of phthisis , and Leonard Colebrook, later distinguished for his work on puerperal fever and on burns Fleming's contributions were the technique of a miniature Wassermann reaction, which gave very good results , a medium for, and the production of a vaccine for, acne , and the use for the first time in England of 'Salvarsan,' Ehrlich's no 606, in syphilis Ehrlich had given Wright a quantity of the drug for experimental use Fleming's results were good, and I recall a sketch a kilted soldier standing to attention with a syringe and edle as big as a rifle and bayonet above the legend rivate 606' '

Before the first world war Fleming had started private actice in Devonshire Place, where besides vaccine and neral bacteriological work he developed the serology of nereal disease and the use of salvarsan in treatment ut all this stopped with the outbreak of war, and eming was soon with Wright in Boulogne as one of team studying modern methods of treating war ounds. His well known work on the use and abuse of ntiseptics started there, and later he was sent to carry further in a large hospital in Wimereux specialising femur wounds A B P who shared the same hut r a year, writes :

> "We were overwhelmed with the work of investigating d treating these wounds gas gangrene being one of the rrible complications and at that time too the influenza idemic caused hundreds of deaths. Blood transfusion by e citrate method was started there by us, and Fleming d ample opportunity to exercise his exceptional talents in e study of wound and septicæmic infections. His notes ere always precise and clear in his very neat handwriting d his graphs and charts covered the walls of our hut boratory His industry was untiring and he was always on e look out for new ideas, or stunts as he called them. At e same time we managed to have fun He laid out a tting-green which was used occasionally at night with ndles in the holes.

After the war Fleming did not take up private practice gain but became assistant director of the inoculation epartment at St. Mary s and professor of bacteriology n the Medical School. He was a good, if not impressive, cturer, but his most valuable quality as a teacher was is friendliness and willingness to help He took great rouble and would often advise a form of technique with ll details written out at length in his own hand As ir Almroth Wright took a less active part in running he institute, Fleming had more and more administrative ork to do But he did not allow his research to be isturbed From 1922 to 1924 he was particularly ngrossed with lysozyme one of the body s natural rotective agents which he discovered when investigating he bacteriology of a cold he had caught In 1929 the iscovery of penicillin was announced as a series of ypically accurate deductions based on a casual observation. His investigations of the antiseptics were continued n a comparison of their antibacterial and antileucocytic owers and led on to his studies of the sulphonamides.

After the development of penicillin at Oxford in the ar years Fleming was inevitably drawn from his boratory to receive the honours accorded him by niversities, cities and nations for the world, with ood reason wished to give him thanks With Howard lorey and E B Chain he received the Nobel prize for edicine in 1945 His honorary degrees ranged from nceton to Louvain He was a freeman of Darvel and f Verona an honorary chief of the Kiowa tribe and member of the Pontifical Academy of Sciences is presidencies included the Society for General icrobiology and the London Ayrshire Society In 944 he was created a knight bachelor His own olleagues in sciences and medicine had elected him R.S in 1943 and F R C.P in 1944 He had received the oxon medal of the Royal College of Physicians, the ameron prize of the University of Edinburgh and the old medal of the Royal Society of Medicine Towards ll these awards his attitude was characteristically odest but some gave him special pleasure including (as V Z C recalls) the medal given him by the Pope in personal interview

"From more humble folk there also came remarkable idence of the universal gratitude He was much moved hen on one occasion as he dismounted from a train at a ation in Spain he found the people on the platform kneeling down as he approached He was also proud of the illuminated message of congratulation and thanks sent him by a group of girls in a school in the Middle West of America. With all his distinctions he remained unspoilt Perhaps the best testimony of this is to be found in *Who s Who* where he placed at the end of his long list of honours a final entry clearly meant to cap the lot Private in the London Scottish for 14 years '

At St Mary s and in London Fleming's professional work and interests continued. In 1947 on Wright's death he became director of what was soon to become the Wright Fleming Institute In this position he stimulated research and instituted demonstrations as a regular thing so that juniors could inform every other department about the type of work they were doing From 1945 to 1948 he was a member of the Medical Research Council and from 1946 onwards he was chairman of the committee responsible for arranging trials of streptomycin and other antibiotics in non tuberculous conditions. Last year he resigned from the directorship of the institute, but he did not retire from the institute Only the day before he died he was planning with his colleagues research in natural immunity which he hoped to begin on his return from a lecture tour in the Middle East

Another thread of Fleming's life lay in Chelsea where he lived for many years. Himself an artist of talent he was elected an honorary member of the Chelsea Arts Club in the '20s and as G F B says, he was an active member

> Winter and summer for over thirty years he would slip unobtrusively into the long low building in Old Church Street about six o clock soon to be embroiled in a desperate struggle at billiards or snooker He was no mean performer his concentration on the shot was ferocious and it was reinforced by a stream of telling badinage directed against his opponents Meantime between shots, he was accessible to all Thanks to him and his colleagues at St Mary's hundreds of artists found help from medicine or surgery and indeed it was an axiom at the club—' if there is anything seriously the matter ask Sandy As the years went by he seemed to grow younger not older and as his honours increased he grew if possible, simpler and more modest.
>
> "Inevitably he posed for many of his friends, though, curiously he eluded most of them Probably the best portrait is that painted by the late T C. Dugdale R.A. but perhaps the best rendering of the essential Fleming is the bust by E. R Bevan. A head by Dyson Smith also has considerable charm

But the centre of his life was of course the Wright-Fleming Institute, and his colleagues there knew him best of all For them R C writes :

> Fleming had most of the qualities that make a great scientist : an innate curiosity to find out how things work, insight into the heart of a problem, ingenuity in devising simple apparatus and simple experiments to test new hypotheses persistence in seeing the job through, and that physical and mental toughness which is essential to the top class investigator He also had to an unusual degree the seeing eye that observed what many of us would miss.
>
> He carried his curiosity into everything he did whether at work or play Only two days before he died he received a stereoscopic projector for his colour films—for he was a keen and expert photographer—and took considerable pleasure in assembling this toy and demonstrating it to us His insight was rather that of the pragmatic mind which sees particularly the practical applications resulting from the solution of a problem His ingenuity in devising simple apparatus was one of his outstanding assets ; neat and deft with his hands, he was a superb technician and it was always a pleasure to watch him at work on the bench. He it was who devised or perfected many of the capillary and glass-slide techniques that became an integral part of the Almroth Wright school of microbiology, and it gave him great pleasure to hear Sir Macfarlane Burnet acknowledge his debt to these micro-techniques. Fleming held very strongly the view that the laboratory worker should be his own technician.
>
> His persistence might be part of an inherited Scottish trait ; certainly he was most unwilling ever to admit defeat. But, if baulked he had a flexibility of mind that a

him to try another tack He had also great powers of endurance Short and stockily built, with powerful square shoulders and a deep chest, he kept his freshness and jaunty step to the end He was not an easy man to know taciturn and laconic, conversation with him was apt to be short and one sided Yet he was fond of people and, even before he became famous, had many good friends in different walks of life

"Despite his frequent journeyings abroad, he maintained his laboratory interests and was making new and interesting discoveries to the end"

Sir Alexander Fleming's first wife, Miss Sarah McElroy, died in 1949 They had one son who is a doctor His second wife, Dr Amalia Coutsouris, whom he married in 1953, was with him when he died from a heart attack on March 11 He is to be buried in St Paul's Cathedral

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# Diary of the Week

MARCH 20 TO 26

### Monday, 21st

HUNTERIAN SOCIETY
8 30 P M (Talbot Restaurant, London Wall, E C 2) Sir Daniel Davies, Dr Donald Reid Dr F H K Green An Assessment of Some New Drugs

### Tuesday, 22nd

ROYAL COLLEGE OF PHYSICIANS OF LONDON, Pall Mall East, S W 1
5 P M Prof W Melville Arnott Order and Disorder in Pulmonary Function (Second of two Oliver-Sharpey lectures)
UNIVERSITY OF LONDON
5 30 P M (London School of Hygiene and Tropical Medicine, Keppel Street, W C 1) Prof Lestor Cahn (Columbia) Oral Medicine
ROYAL SOCIETY OF MEDICINE 1, Wimpole Street, W 1
8 P M *Medicine* Dr H A Sissons, Dr Paul Fourman Dr C E Dent Osteoporosis
INSTITUTE OF DERMATOLOGY, St John's Hospital, Lisle Street, W C 2
5 30 P M Dr G C Wells Pigmented Tumours

### Wednesday, 23rd

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields W C 2
5 P M Prof W W Mushin Measurement in Anæsthesia (Joseph Clover lecture)
GUY'S HOSPITAL MEDICAL SCHOOL St Thomas' Street S E 1
5 P M. Sir Lionel Whitby Evolution of the Treatment of Addison's Anæmia (Addison lecture)
ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE, 28 Portland Place, W 1
3 30 P M Dr J H Sheldon Social Aspects of Old Age
INSTITUTE OF DERMATOLOGY
5 30 P M Dr Henry Haber Cellular Nævi and Melanomas
INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Road W C 1
5 30 P M Dr Imrich Friedmann Otitis Media—Experimental and Human (Second of two lectures)
INSTITUTE OF ORTHOPÆDICS, Royal National Orthopædic Hospital, 234 Great Portland Street, W 1
8 P M Prof. O Scaglietti (Florence) Closed Treatment of Congenital Dislocation of the Hip
EUGENICS SOCIETY
5 30 P.M (Royal Society, Burlington House, W 1) Dr Hilda Lewis Inadequate Parents and Psychological Disorders in their Children

UNIVERSITY OF OXFORD
5 P M (Radcliffe Infirmary) Prof C H G Macafee Solid Ovarian Tumours
MANCHESTER MEDICAL SOCIETY
4 30 P.M (Medical School) *Medicine* Dr James Sharp Differential Diagnosis of Ankylosing Spondylitis
LIVERPOOL MEDICAL INSTITUTION, 114 Mount Pleasant Liverpool, 3
8 P M *Pathology* Dr G R Wadsworth Effects of Hæmorrhage in Man Dr S E Keidan C-reactive Protein
BIRMINGHAM MEDICAL INSTITUTE 154 Great Charles Street, Birmingham, 3
8 P M *Psychiatry* Dr J M. Jefferson Mr J T Allanson, M.SC, Mr P T Geach Mind and Body

### Thursday, 24th

INSTITUTE OF DERMATOLOGY
5 30 P M Dr R W Riddell Epidemiology of Fungous Diseases

### Friday, 25th

ROYAL COLLEGE OF SURGEONS OF ENGLAND
5 P M Prof Robert Bradlaw De Cute Oris (Hunterian lecture)
ROYAL SOCIETY OF MEDICINE
5 P M *Epidemiology and Preventive Medicine* Dr J A H Lee, Dr Josefine Webb National Service Medical Examinations and Epidemiological Research
8 15 P M *Obstetrics and Gynæcology* Mr E Parry Jones, Mr Alistair Gunn Use of Kielland's Forceps
INSTITUTE OF LARYNGOLOGY AND OTOLOGY
3.30 P M Mr K. G Rotter Aural Vertigo
ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASGOW, 242 St. Vincent Street
5 M Prof E J Wayne Clinical Surveys and Clinical Trials

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# Notes and News

## MENTAL NURSES REFLECT ON THEIR JOB

THE staff college for ward sisters, set up some years ago by King Edward's Hospital Fund for London, has just held a course for sisters and male charge nurses from mental hospitals This was a new departure, being not only the first course for mental hospital staff, but the first mixed course, to be held at the college, and it has been an unqualified success Lectures, followed by discussions, ranged over hospital and ward administration, the care of patients, and the training of nurses, and visits were made to various mental and mental defective hospitals, to Roffey Park Rehabilitation Centre, and to the psychiatric department of a general hospital It is always interesting and a little sobering to see what other people are doing a mildly complacent confidence, among the members, that all was well and fully up to date in their own hospitals, was replaced, as the course proceeded, by a healthy uncertainty and many asked for advice on the best ways of putting new ideas across to their colleagues, when they got back

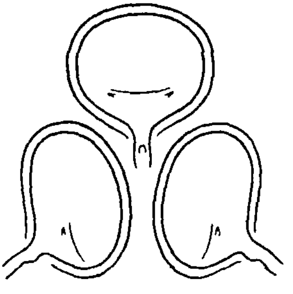
A final discussion on the value of the course was warmly favourable all felt they had learnt much which they would be able to use in their work The relation of the sister tutor and the ward sister in their joint task of training nurses, was discussed at this session, and it was generally felt that these two prime educationists were too far separated by custom and practice They need to be in much closer touch with each other Sister tutors were said to be too academic in their training, perhaps prescribing standards which it would be impossible to maintain in the wards In the absence of sister tutors the other side of the argument could not be put, but the suggestion that the ward sister should have a say in the training syllabus seems thoroughly reasonable It was also suggested that, before being appointed to charge of a ward, a sister might well spend a short period—a week perhaps—in the sister tutor's department Another proposal was that ward sisters should be able to meet and discuss nurse training with the tutor either on an educational committee or at weekly meetings of a procedure committee At all events, members of this course were determined that they were going to make closer touch with their sister tutors when they returned to their hospitals

There was general agreement that, from the student nurse's point of view, case assignment adds greatly to the interest of the work, and might—if coupled with better training—help to reduce wastage There are special difficulties, however, about arranging case assignment in mental hospitals, for student nurses are off for two full days every week Group assignment—in which several patients are assigned to the care of a group of nurses, headed by a staff nurse or a third-year student—would be more feasible and probably more satisfactory

Many of the members were working under unfavourable conditions Most of our mental hospitals are old and out of date, and in many of them sanitary annexes are inadequate and inconvenient and cleaning equipment primitive In the past, lack of money has caused delay in introducing improvements, but this no longer holds Reasonable expenditure on the mental hospitals is being encouraged by the Government, and the King's Fund have already made generous grants towards improvements Members of the course felt that they had been accepting inconveniences with rather too much resignation, and that the time had now come for them to press for improvements In many places extra amenities for the patients are now being provided by "friends of the hospital", but such leagues of friends are by no means universal, and there seems to be no fixed plan for establishing them One member of the course had had the initiative to start such a league herself, beginning with friends and relatives of patients in her own ward, and it is to be hoped that others will follow her lead Apart from the direct benefit to patients and staff of an active league of friends, there are indirect benefits a strong league of friends can help to break down prejudice against mental hospitals, spread information among the general public, and reduce substantially the objection many parents feel to allowing their daughters to enter mental nursing

## CYSTOSCOPY DIAGRAM STAMP

Mr Alec W Badenoch, F.R C.S, writes For noting findings made at a cystoscopy some surgeons use separate charts but these are expensive and bulky To record successive



observations on say a case of bladder neoplasm, I find a diagrammatic representation of the bladder useful With most bladder stamps it is difficult to indicate the presence of seedlings near the internal urinary meatus especially when the growth is on the anterior wall or in the posterior urethra The composite stamp illustrated obviates this difficulty and allows the surgeon to record whether the growth has extended into or through the bladder wall

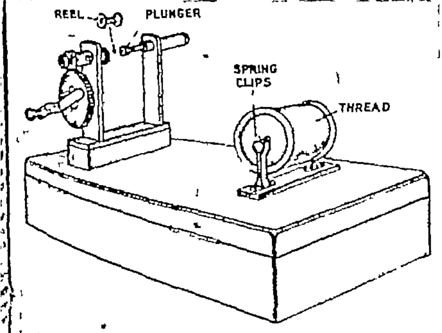
I have to thank Miss Wadsworth of the Institute of Urology for making the final drawing The stamp was cut by and can be obtained from, Messrs. E M. Richford 6 Snow Hill London, E.C.1

## ECONOMIES IN DRUGS AND DRESSINGS

In a letter to hospital authorities [1] the Ministry of Health discusses ways of cutting expenditure on drugs and dressings. Though some 3000 different drugs are used by most general hospitals, four fifths of the total expenditure is usually accounted for by 30 main items and the Ministry suggests that hospital medical committees should investigate the prescribing of these items with a view to effecting economies. The more expensive antibiotics should be used only when strictly necessary and vitamins should not be prescribed routinely except for sound medical reasons. Before prescribing expensive surgical dressings (e.g gauze) the cheaper alternatives should first be considered and non proprietary preparations wherever these are cheaper should be prescribed rather than proprietary preparations Since many drugs deteriorate if unsuitably stored ward stocks should be kept small, and the pharmacist should check them regularly The Ministry suggests that a standing committee with representatives from the medical pharmaceutical and nursing staff should be set up in each hospital to advise on these matters.

## A NEW LIGATURE WINDER

Mr R N Jones writes : "Winding reels of ligature material by hand is laborious, and even with experience the results are not always to the surgeon s satisfaction The machine shown in the accompanying figure was devised by Mr D W Vincent instrument technician to Colchester hospital group It does the job simply and rapidly ; and since it winds at an even tension the ligature is smooth running and less likely to break when in use Reels of any size can be wound ; they are held in place by a plunger



The winder is made by the Electro Surgical Instrument Company Ltd, 37A New Cavendish Street London W 1

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[1] 91151/3/51 dated March 3 1955

### University of Cambridge

On March 5 the following degrees were conferred

*M Chir.*—G R C Peatfield
*M.B B Chir*—A M. Freeman, *George Yerbury
*M B*— Inez R. Aldous J A Dryden, R. J C. Pearson.
By proxy

### University of London

Honorary fellowships of University College have been conferred on Prof A Bradford Hill F.R.S Dr A J Morland and Prof Solly Zuckerman F R.S

### University of Birmingham

Mr A L D Abreu part time lecturer in surgery has been given the title of reader in thoracic surgery, and Dr W Trevor Cooke has been appointed part time reader in medicine on giving up his appointment as reader Mr A J H Rains Mr P G Bevan and Mr Geoffrey Slaney have been appointed lecturers in surgery Mr Slaney has been awarded the first Frank Barnes travelling fellowship in America

On Wednesday and Thursday May 11 and 12 at 6 P.M Prof Wilfrid Gaisford will give the Leonard Parsons lecture on the Protection of Infants against Tuberculosis.

### University of Nottingham

At a congregation to be held on April 22 for the installation of the Duke of Portland as chancellor of the university the honorary graduands will include Sir Henry Cohen who will receive the degree of D.SC

### Royal College of Surgeons of England

At a meeting of the council on March 10 with Sir Harry Platt the president in the chair Sir Geoffrey Marshall was awarded the Tudor Edwards lectureship for 1955 The second Lady Cade medal was awarded to Squadron Leader Peter Howard and the Hallett prize to D Singh (Patna)

### Royal College of Physicians of London

On Tuesday and Thursday April 19 and 21, Dr A. M Cooke will give the Lumleian lectures on Some Aspects of Skeletal Disease On Tuesday and Thursday May 3 and 5 Sir Horace Evans will give the Croonian lectures on the Significance of Certain Symptoms in Disease of the Kidneys. All the lectures will be held at 5 P.M at the college Pall Mall East S W 1

### Royal College of Physicians of Ireland

The following have been admitted to the membership

Kale Mohan Basu (in absentia) W R. Shanahan O M P Tobias

### Royal Society of Edinburgh

*The David Anderson Berry Medal and Prize* (£100) will be awarded in 1956 by the society for the best work on the therapeutical effect of X rays on human diseases. Further particulars may be had from the general secretary of the society 22 George Street Edinburgh 2

### University of Melbourne

Mr Maurice Ewing senior lecturer in surgery at the Postgraduate Medical School of London has been appointed to the new chair in surgery in this university

Mr Ewing who is 43 years of age was educated in Edinburgh at Daniel Stewart s College and at the university He graduated in 1935 with honours and was awarded the Ettles scholarship After holding house-appointments in Edinburgh and Leicester he joined the R.N V R. in 1940 and served till 1946 with the rank of surgeon lieut -commander After demobilisation he held appointments as tutor at the Edinburgh Royal Infirmary and at the Victoria Infirmary Glasgow before he took up his present appointment in 1947 In 1950 he worked at the Memorial Hospital in New York with a British American exchange scholarship His published works have dealt mainly with proctology and the management of malignant disease of the mouth In 1950 he gave a Hunterian lecture on villous tumours of the rectum.

Dr R R H Lovell, senior lecturer in medicine at St. Mary s Hospital Medical School has been appointed to the new chair of medicine

Dr Lovell who is 36 studied medicine at St Mary s Hospital Medical School qualifying in 1941 During the remaining years of the war he served as a surgeon lieutenant in the R.N V R. and was mentioned in despatches After demobilisation he held a house-appointment at the Brompton Hospital and a registrarship at St. Mary s Hospital, He took the M.R. in 1946 the M.R.C.P in 1947 and the M.D in 1948 He was awarded a Nuffield lectureship to visit North America in 1953 During the last five years he has been concerned with the investigation of connective ti sue and the mode of action of cortisone His published work papers on clubbing of the fingers the modification of in by cortisone and other substances and the d of discovered in the serum of patients with which causes necrosis when injected in guin

### Royal Institute of Public Health and Hygiene

The Harben medal has been awarded to Lord Adrian, O M, P R S, and the Smith award to Dr Kenneth Cowan

### National Association for Maternal and Child Welfare

The annual conference of this association will be held at Church House, Westminster, on June 23 and 24 Further particulars may be had from the secretary of the association, Tavistock House North, London, W C 1

### Symposium Neuroradiologicum

This meeting will be held in London from Sept 13 to 17 The programme includes discussions on cerebrovascular disease, the localisation of intracranial tumours by means of isotopes, and applications of stereotaxometry Further information may be had from Dr R D Hoare, The National Hospital for Nervous Diseases, Queen Square, W C 1

### Association of Surgeons of Great Britain and Ireland

This association will hold its annual meeting in Glasgow from April 14 to 16, under the presidency of Sir Clement Price Thomas There will be discussions on Obstructive Jaundice, Postoperative Care, and Occlusive Vascular Disease Further particulars may be had from the secretary of the association, 45, Lincoln's Inn Fields, W C 2

### Royal Australasian College of Surgeons

*Alan Newton Prize*—The subject chosen for the next award of this essay prize is the Pathogenesis and Surgical Treatment of Developmental Abnormalities of the Kidneys and Ureters Candidates must be fellows of the Royal Australasian College of Surgeons, the Royal College of Surgeons of England, the Royal College of Surgeons of Edinburgh, or the Royal College of Surgeons in Ireland, or fellows in surgery of the Royal Faculty of Physicians and Surgeons of Glasgow Entries must be sent to the secretary of the college, Spring Street, Melbourne, C 1, by Dec 1, 1956

### University of Saskatchewan

This university has lately expanded its medical school, and medical students may now complete their clinical training in Saskatoon A university hospital of 550 beds has been opened and five full time chairs established The new professors are Dr J W Gerrard (pædiatrics), Dr Eric Nanson (surgery), Dr Irwin M Hilliard (medicine), Dr Albert E Brown (obstetrics and gynæcology), and Dr D G Mckerracher (psychiatry) The dean of the school is Dr J Wendell Macleod

Dr Gerrard who is 38 was born in Northern Rhodesia He studied medicine at Oxford and Birmingham, graduating B M in 1941 He spent the remaining years of the war as a regimental medical officer and in 1946 he returned to Birmingham as R.M O at the Children's Hospital While working under Dr L M Masterman at the Selly Oak Hospital he took the M R.C P in 1947 Later he was appointed medical registrar at the Children's Hospital, and in 1948 he took up his present post Last year he spent six months in the United States working under Dr Lawson Wilkins at Johns Hopkins Hospital Baltimore His published work includes a study of the natural history of kernicterus and papers (jointly) on the treatment of phenylketonuria and of cœliac disease

### McGill University, Montreal

Prof R V Christie has been appointed professor of medicine and chairman of the department of medicine in the university He has also been appointed physician in chief of the Royal Victoria Hospital, Montreal

Professor Christie who is 52 years of age, was educated in China and at George Watson's College, Edinburgh He graduated M B at the University of Edinburgh in 1925 and, after holding house appointments at the Edinburgh Royal Infirmary he went to New York as assistant in the department of applied physiology of the Rockefeller Institute for Medical Research and in 1927 was awarded the Gunning Victoria Jubilee prize for his investigations there The following year he moved to Montreal to become resident medical officer at the Royal Victoria Hospital In 1929 with a Travers Allan scholarship he spent some months in Freiburg under Aschoff On his return to Montreal he was appointed research associate in the McGill University research clinic of the Royal Victoria Hospital He returned to this country in 1935 on his appointment as assistant director of the medical unit of the London Hospital In 1937 he was awarded the gold medal of the University of Edinburgh for his M D thesis He was appointed to the chair of medicine at St Bartholomew's Hospital in 1938 In 1942 he took the D SC Lond. and the same year he was elected F R.C P The following year he delivered the Goulstonian lectures of the Royal College of Physicians, on emphysema Dr Christie is a member of the senate of London University His published work includes papers on respiratory function in disease and the use of antibiotics in subacute bacterial endocarditis

### Breeding of Laboratory Animals

The Laboratory Animals Bureau will hold a symposium on this subject at 1, Wimpole Street, London, W 1, on Monday, May 9, at 10 A.M This symposium is open to scientific, medical, and veterinary graduates, and to senior technicians

### Medical Society of London

At this society's 175th anniversary dinner, held at the Royal College of Surgeons of England on March 8, the Duke of Gloucester remarked that Lettsom, in founding the society had aimed to enable members of the profession to meet on terms of equality in order to discuss matters of common interest, and the Lettsom tradition had helped to keep the society active and strong In reply, Sir Horace Evans, the society's president, gave evidence of the society's continuing and growing strength meetings, he said, were well—some times uncomfortably well—attended He recalled a further remarkable feat by Lettsom In an age when the sick poor were treated "with a callousness impossible to believe," he had founded a dispensary, the first of its sort, on which patients could call for domiciliary visits by consultants Sir Harry Platt, P.R C S, responded to Dr E R Cullinan's cordial and witty welcome to The Guests

### Hunterian Society

On March 10 this society formally presented to the Royal College of Surgeons the coat-of arms of John Hunter, which, with that of Lister, is incorporated in the balcony of the gallery of the college's new great hall In handing over the arms, Dr W S C Copeman, the president, described them as a gift from "our society to your society" Though divided over the date of Hunter's birth, which the Hunterian society celebrates on Feb 13 and the college on Feb 14, they were united in honouring the man and his work Dr Copeman could not but admit a certain difficulty in that John Hunter had no coat-of arms, and the one appearing in the balcony was actually that of his brother, William Hunter In no way discomposed by this revelation, and overlooking the inaccuracy of the society's research on birthdays, Sir Harry Platt, P R C S, gratefully accepted the arms on behalf of the college, and said that a plaque would be placed in the hall to commemorate the gift

CORRIGENDUM *Pharmacology of Reserpine*—In this leading article last week (p 548) the footnote numbered 26 should have appeared as 25, and that numbered 25 as 26

## Appointments

BROCK B H, M B Camb, F R.C.S registrar in orthopædic and traumatic surgery Winford Orthopædic Hospital, and United Bristol hospitals

CARROLL, JAMES, M B N U I D P H. D O H. district M O H and asst county M.O H. Burton Latimer Corby Desborough, and Rothwell urban districts and Kettering rural district.

CLEMENTS P A H, M R.C S asst senior M O, headquarters staff of the East Anglian R.H B

GAMAN, R. H, B M Oxfd D P M consultant psychiatrist and medical superintendent Risbridge Hospital Kedington, and Riversfield Home, St Neots

GOWANS J A L.R C P E senior casualty officer, Wansbeck H.M C.

GRIFFITH A. H M.B Lond, D P H senior M O Cardiff

GRIFFITHS, J J, M R.C S, T D D whole time asst chest physician, mid Wales group

HAIGH, R D, M B. Leeds, D P H, D OBST senior asst M O, Brighouse Corporation Elland urban district council, and West Riding county council

MASON R M, D.M Oxfd M R.C P consultant physician, department of physical medicine London Hospital

METGUD, V S, M B Bombay, F R.C S E. senior casualty officer, Tees side H M C

O CONNELL J J O B E., M B N U I, D M R D radiologist, Tipperary (S R.) county council

PRICE MARY, M B. school M O and asst M.O H Brighton

STAFFORD CLARK DAVID M D Lond M R C P physician-in charge department of psychological medicine, and director of the York Clinic, Guy's Hospital London

WOLMAN LIONEL, M D Camb, M R C P D P M consultant neuro pathologist Royal Infirmary Unit, United Sheffield Hospitals

**The Hospital for Sick Children, Great Ormond Street, London**

BAMFORD, F N M B Manc. house-surgeon
CHEESE J A M D Lond D C H house physician
STEPHENS ROSEMARY, M B Lond, D C H house physician
VUCKOVIC DRAGOMIR, M B Birm house physician, neurological and neurosurgical department

**Appointed Factory Doctors**

DAWE, E B M R C S Ventnor Southampton
WOOD L A C M.B Camb, D OBST Penshurst Kent.

# ASSESSMENT OF BLOOD-LOSS IN CIVILIAN TRAUMA

RUSCOE CLARKE
M.B.E., M.B Lond F R C.S
SURGEON BIRMINGHAM ACCIDENT HOSPITAL

ELIZABETH TOPLEY
M D Lond
MEMBER OF M.R.C INDUSTRIAL INJURIES AND BURNS RESEARCH UNIT

CECIL T G FLEAR
B Sc M B Birm
GE SURGEON BIRMINGHAM ACCIDENT HOSPITAL MEMBER
M.R.C INDUSTRIAL INJURIES AND BURNS RESEARCH UNIT

THE effective use of efficiently cross-matched blood the emergency treatment of trauma is limited by ifficulty in assessing the amount of blood lost and by ck of clarity on the optimal extent and timing of its placement. Blood transfusion can be used in trauma ot only to control overt patterns of clinical "shock ut also to prevent degrees of oligæmia and anæmia which av contribute to the "illness of trauma" both in the cute phase and during the ensuing weeks We attempt ere to define the degree of blood loss in certain civilian juries.

During the 1939–45 war many workers—e g Grant nd Reeve (1951), Emerson and Ebert (1945) and Noble nd Gregersen (1946)—found greater blood loss than had reviously been recognised and recommended the ansfusion of larger quantities of blood They tried to orrelate blood volume with blood loss from the wound hough blood loss to the exterior can rarely be measured curately it appeared that total blood loss from war wounds could be roughly gauged by consideration of the ature and extent of local injuries, at least when they ere confined to the extremities

Noble and Gregersen (1946) state that in skeletal auma

> the total amount of blood loss will in general depend on e extent of muscle contusion upon the number of fractures d upon their relation to blood vessels.
>
> er estimations of blood volume showed that a single ajor fracture was likely to be associated with a reduc n of blood volume of about 20% two major fractures th a reduction of 20–40% and three or more such frac es with a reduction of more than 40%

Grant and Reeve (1951) found the volume of damaged ue to be a valuable index of blood loss They took a unit of volume the patient s hand—the closed fist r deep wounds, and the open hand for surface wounds nd divided wounds into four categories

> (1) *Small wounds* with tissue damage of less than 1 hand ood-loss less than 10% rarely more than 20%.
>
> (2) *Moderate wounds* with tissue damage of 1 or more but than 3 hands: blood loss 20–40%.
>
> (3) *Large wounds* with tissue damage of more than 3 but less an 5 hands: blood loss about 40%
>
> (4) *Very large wounds* with tissue damage of 5 hands or ore blood loss about 50% or more

se workers recognise the crudeness of their approach d state that they

> came to rely on it more and more and that when we dealt h abdominal injuries where this was not available our ical assessments of blood loss were more often at fault und size is of particular value as a sign because it is not e blood pressure and other circulatory phenomena liable be affected by other factors.

One of us (Clarke 1952) attempted to assess blood loss civilian injuries from hæmoglobin levels during the ensuing two weeks with occasional plasma volume studies and was convinced that blood was lost in civilian injuries even in closed fractures, in amounts comparable to that lost from the more obviously damaging wounds of war

We report here studies of blood loss in closed and open injuries, emphasising the relevance of limb swelling In contrast to earlier workers we have deliberately delayed blood volume studies until at least twenty four hours after injury We have used the red-cell volume at this time as the index of whole blood credit or deficit. Hb levels during the following two weeks provide further evidence of this whole blood credit or deficit These results combined with the knowledge of the volume of blood transfused, provide a guide to total blood loss

## Methods

### RED CELL VOLUME

Red-cell volume plasma volume, and venous hæmatocrit were estimated in 22 cases from one to four days after injury We have assumed that any changes in the red-cell volume during the first four days after injury are likely to be due to two main factors blood loss from injury, and blood replaced by transfusion The red-cell volume during this period is probably not greatly affected by new formation of red cells (Topley et al 1955) In contrast the plasma volume can change by hæmodilution and thereby alter the Hb level, &c. in the peripheral blood Primary consideration was therefore given to the red cell volume rather than to whole blood volume

We express red-cell volume in terms of whole blood so that it can be correlated with measurements of blood transfused, blood loss to the outside and limb swelling which may be due to blood loss. We have assumed that blood lost from the site of injury had a hæmatocrit of 40%, and that each bottle of blood transfused (540 ml including anticoagulant) contains about 440 ml. of donor blood of which about 400 ml reaches the patient One bottle therefore provides 0·4 litre Thus the whole blood loss in litres at the time of a red-cell volume estimate from one to four days after injury is

$$\frac{\text{(predicted normal red-cell volume in litres—1–4 day red-cell volume in litres)}}{0{\cdot}4} + \text{(bottles of blood transfused} \times 0{\cdot}4)$$

The technique of estimating red-cell volume was, except where otherwise stated the radioactive $^{32}$P red-cell volume method of Reeve and Veall (1949) with Chaplin's (1954) modification In a few instances we derived an estimate of red-cell volume from the Evans blue plasma volume and venous hæmatocrit

*The predicted normal red-cell volume* was usually calculated from both the follow up weight and the $^{32}$P red cell volume occasionally from pre injury weight or follow up height For males we have allowed 30 ml red cell volume per kg of body weight For females and whenever height has been used we have used the data of Gibson and Evans (1937) adding a correction for body/venous hæmatocrit ratio

The impossibility of knowing the pretraumatic blood volume reduces the accuracy of the estimated red-cell volume deficit In more serious injuries the blood volume may not return to normal even after prolonged convalescence In injuries with permanent disability and loss of muscular tone it may never return to pre-accident level—e g case 35

Usually the $^{32}$P red-cell technique from one to four days after injury can reasonably be used for analysis of blood loss The red-cell volume derived from the Evans-blue and venous hæmatocrit is often of the same order of accuracy though occasionally misleading (Topley et al 1955)

### HÆMOGLOBIN

From admission onwards repeated tests were made on the peripheral blood by the oxyhæmoglobin method The lowest Hb level during this period is regarded as further evidence of whole blood deficit or credit at end of emergency treatment For example in of relatively severe injuries all the patients whose Hb level fell more than 30% below normal had a red cell volume deficit of at least 20% below normal by the second or third day, whereas all the patients who never became anæmic had a red cell volume credit at the end of emergency treatment

### LIMB SWELLING

We measured the increased size of injured limbs by comparison between the injured and normal Two methods were used, the first involving fluid displacement, and the second serial circumferential measurements Both are suitable for closed fractures, the second can also be used for open fractures

*Fluid Displacement Method*

The injured limb is immersed in a 'Perspex' tank so that a line marked circumferentially on the limb at a known distance from a bony landmark corresponds to the level of water in the tank This is next marked off on the tank The injured limb is removed, and the normal limb is placed in the tank With this limb immersed to a mark at a similar level, water is added so that the level comes up to the mark on the tank The amount of water added equals the difference in volume between the two limbs

The accuracy of this method was tested in 20 normal adult males At a point 4 inches below the tibial plateau there was a mean difference of 19 ml between the right and left legs (S D ± 25 9 ml), at a point 9 inches below the tibial plateau the mean difference was 11 ml (S D ± 21 1 ml) For practical purposes the method is probably accurate to within 50–75 ml in any individual case

*Circumferential Measurement*

Measurement of swelling in this way (Cotterill 1951) involves circumferential measurements over a length of the injured and normal limbs, at 2 cm intervals, starting from a fixed bony point With this information it is possible to calculate the difference between the summated volumes of a series of imaginary cylinders Since the limb is not circular on cross section, this approach underestimates the actual volume and, since the swollen limb is more nearly cylindrical, it underestimates the difference still more Nevertheless it provides a guide of considerable use for this purpose Clearly it is unreliable in the presence of gross shortening from a fracture with overlap, and cannot be applied until this has been corrected

The accuracy of this method using an ordinary tape measure was checked by repeated measurements on six normal people The mean difference between the two limbs was 154 ml (S D ± 76 6 ml) for the thigh and 66 ml (S D ± 36 6 ml) for the leg For practical purposes it is probably accurate within 250 ml for the thigh and 150 ml for the leg

The limb swelling in one patient was measured by fluid displacement and circumferential measurement methods, and substantial agreement was found

### SIGNIFICANCE OF LIMB SWELLING

Numerous workers (Blalock 1930, Parsons and Phemister 1930, Freedlander and Lenhart 1932, O'Shaughnessy and Slome 1935, Slome and O'Shaughnessy 1938, Ashworth et al 1944, Nickerson 1945, Phemister and Laestar 1945) have measured the volume of swelling associated with experimental injuries and have tried to correlate it with the general reactions of the organism and with blood-volume changes We have been unable to find any similar attempt in accidental injuries of limbs in man

We are concerned not only with the volume of swelling but also with its composition In theory such swelling could be due to whole blood, exudation of plasma, or increased circulating fluid in the vessels Other extracellular or intracellular swelling is less likely The over all composition of the swelling probably changes with the passage of time and varies with the species and the nature of the injury

In animals such swellings have been variously estimated to contain 25–100% of whole blood The common civilian injuries of man are associated with tearing and torsion of blood vessels, opening up tissue space rather than inflicting direct violence to the tissues

We suggest that in the acute stage of human injury—i e, within the first 6–12 hours—the swelling consists largely of whole blood Our impressions are supported by the following additional considerations

(1) At operation on closed fractures during this period larg amounts of blood are found in the region of the swelling

(2) At operation during this same period tissues are norma in texture by contrast with their appearance when expose to surgery at a later stage Œdema or exudate is rarely seen

(3) In major limb injuries due to acute violence and no resulting from prolonged pressure there has been found n evidence of hæmoconcentration suggesting differential loss o plasma from the circulation (Chute et al 1945, Emerso and Ebert 1945, Grant and Reeve 1951)

(4) Many patients with moderate swelling at the acute stag develop widespread discoloration later

(5) The amount of swelling in the closed injuries whic we have investigated corresponds in amount approximatel to the primary loss of whole blood indicated by red-ce volume studies

We are convinced on clinical grounds that the size early local swelling is a valuable guide to blood loss an to the contribution of local damage to the systemic di turbance Further observations are required in ma including studies on red-cell and plasma volume and o the contribution of blood to limb swelling

TABLE I—CLOSED INJURIES BLOOD-LOSS CALCULATED FROM RED-CELL VOLUME

| Case no | Age (yr) | Site of fracture | Weight or height | * Predicted normal blood volume (litres) | Day of R C V | A whole blood deficit (litres) calculated from predicted normal R C V by follow up | | Lowest Hb level on day 4–14 (g per 100 ml) | B blood transfusion (litres) | A + B whole blood loss (litres) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | * (a) weight or height | (b) R C V by ³²P | | | (a) | (b) | Me |
| 1 | 20 | Shaft of femur | 64 kg | 4 8 | 4 | 1 6 | 0 9 | 11 7 | 0 | 1 6 | 0 9 | 1 2 |
| 2 | 65 | Shaft of femur | 65 kg | 4 9 | 1 | 1 8 | 0 9 | 10 2T | 0 | 1 8 | 0 9 | 1 3 |
| 3 | 29 | Trochanter of femur, tibia and fibula | | 4 3$^1$ | 3 | | 2 0 | 8 0T | 0 | | 2 0 | |
| 4 | 34 | Shaft of femur | 63 kg | 4 7 | 1 | −1 3 | −0 9 | 14 7 | 2 0 | 0 7 | 1 1 | 0 [illegible] |
| 5 | 43 | Shaft of femur | 77 kg | 5 8 | 1 | 0 1 | −0 8 | 14 0 | 0 8 | 0 9 | 0 0 | 0 1 |
| 6 | 25 | Shaft of femur ankle 4 and 5 metacarpals | 63 kg | 4 7 | 1 | 0 2 | 1 5 | 13 8 | 0 8 | 1 0 | 2 3 | 1 [illegible] |
| 7 | 62 | Trochanter of femur clavicle, 1st rib | 73 kg $^2$ | 4 0 | 1 | 0 6 | 0 0 | 12 6 | 1 6 | 2 2 | 1 6 | 1 9 |
| 8 | 63 | Ilium | 59 kg | 4 4 | 1 | −0 4 | −0 7 | 13 4 | 1 2 | 0 8 | 0 5 | 0 [illegible] |
| 9 | 55 | Shaft of femur | 171 cm $^3$ | 5 0 | 1 | 0 9 | | 14 7 | 0 8 | 1 7 | | |
| 10 | 15 | Lower femur | 49 kg $^4$ | 3 7 | 1 | 0 9 | | | 0 | 0 9 | | |

R C V red-cell volume ³²P, radioactive phosphorus technique T Hb level before blood transfusion for anæmia

* Predicted normal R C V for males = follow up weight (kg) × 30 (ml) and blood volume = weight (kg) × 75 (ml) with the following exceptions 1 based on follow up ³²P R C V + plasma volume 2, because of gross weight change pre-accident weight was used, and because female figures of Gibson and Evans (1937) were used. 3 because height not weight, was used figures of Gibson and Evans (1937) were used 4, because of gross weight change, pre accident weight was used

### BLOOD LOSS FROM WOUNDS

Blood loss from open wounds cannot be measured before the patient comes under medical care Occasionally we have been able to examine the site of the accident and to gauge the extent of primary bleeding Usually we receive a large proportion of serious accidents within 15–30 minutes of injury and have the impression that early bleeding before arrival at hospital only makes a decisive contribution to total blood loss in a small percentage of cases. Sometimes we can derive a crude estimate from the staining of clothes or of the stretcher on arrival at hospital

Once the patient is in hospital, it is possible to encase the wound area in a 'Polythene' bag fixed to the limb above and below the wound and to collect blood shed between admission and surgery At operation for closed or open injuries blood loss can be determined by weighing the swabs (Baronofsky et al 1940) Such observations have been made on some of the patients reported here Additional estimates were based on the degree of mess on the floor staining of towels gowns &c or the rate of blood drip from the wound.

## Results

### CLOSED INJURIES

The investigation of closed injuries is uncomplicated by blood loss to the outside We have made observations on patients not requiring surgery and without clinical signs of "shock" Many of them would normally not be considered to require transfusion Some have received blood transfusions designed to modify the 'illness of trauma," in amounts varied so that the effects of such variation could be studied.

The evidence of *blood loss from red-cell volume* studies in closed fractures is summarised in table I in which A shows the whole blood deficit or credit—i e , the difference between the measured red-cell volume (day 1–4) and the "predicted normal" red-cell volume derived (*a*) from follow up weight and (*b*) from follow up $^{32}$P red cell volume The lowest Hb level recorded during the ensuing two weeks is included as a further guide to the whole blood credit or deficit B shows the amount of blood transfused. Whole blood loss (A+B) is calculated separately from follow up weight and $^{32}$P red cell volume These results have been arbitrarily averaged

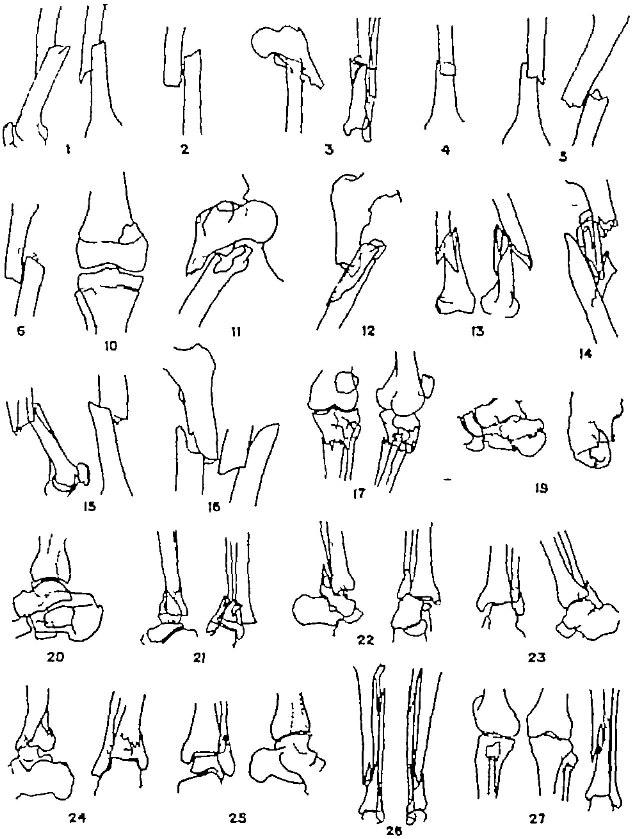

Fig. 1—Tracings of radiographs showing injuries : numerals refer to cases in text and tables.

Case 1 —An airman aged 20 fractured the shaft of his femur (fig 1) At hospital half an hour later his skin was warm and pink and his pulse and blood pressure were normal The fracture was treated by manipulation and skeletal traction under general anaesthesia The primary swelling of the limb was relatively small (table II) and was measured as 0·4 litre The thigh continued to swell for two days. No further interference with the fracture was needed. Total blood loss calculated from red-cell volume on the fourth day after injury was 1·2 litres.

Case 2 —A baker's roundsman aged 65 was knocked off his cart fracturing his left femur (fig 1) and pubic bone On admission his colour and skin temperature were normal pulse-rate 80 and B.P. 120/70 mm Hg Under general anaesthesia the femur was reduced and fixed by skeletal traction Local swelling was estimated to be at least 1·0 litre with additional extravasation from the pubic fracture suggesting total blood loss of about 1·5 litres. The red-cell volume deficit on the day after injury was 1·3 litres.

Case 3 —A man aged 29 knocked down by a car sustained a mild head injury lacerated scalp closed fracture of the left tibia and fibula and comminuted fracture of the upper right femur (fig 1) He was a little pale B.P. 120/90 mm. Hg pulse-rate 80 Under general anaesthesia skeletal traction was applied to the right leg and the fracture of the left leg was manipulated and put in plaster ; the lacerated scalp was sutured Blood loss from the scalp was less than 0·2 litre It was estimated that he had lost 0·75 litre into the left leg and 1·0 litre into the right thigh. He was not transfused Blood loss from red-cell volume on 3rd day was 2·0 litres

Case 4 —A miner aged 34 injured by a fall of coal reached hospital six hours later with a fractured femur (fig 1), which

TABLE II—CLOSED INJURIES LIMB-VOLUME DIFFERENCES BY SERIAL CIRCUMFERENTIAL MEASUREMENTS

| Case no | Age (yr ) | Time after injury (hr ) | Injury | Distal point from which measurements were taken | Distance over which measured (cm.) | Difference in volume (litres) |
|---|---|---|---|---|---|---|
| 11 | 25 | 6 | Subtrochanteric fracture of femur | Tibial plateau | 42 | 1 3 |
| 12 | 48 | 7½ | Fractured upper shaft of femur | Tibial plateau | 38 | 1 6 |
| 13 | 46 | 2½ | Fractured lower shaft of femur | Tibial plateau | 36 | 1 4 |
| 14 | 21 | 2½ | Comminuted fracture of shaft of femur | Tibial plateau | 40 | 2 2 |
| 15 | 70 | 5½ | Fractured mid shaft of femur | Tibial plateau | 40 | 1 2 |
| 16 | 55 | 3 | Fractured upper shaft of femur | Tibial plateau | 40 | 0 4 |
| 1 | 20 | 3 | Fractured lower shaft of femur | Tibial plateau | 44 | 0 4 |
| 10 | 15 | 14 | Fractured lower femur | *Lateral malleolus* | 40 | 1 2 |
| 17 | 66 | 7 | Comminuted fracture of tibia and fibula into knee joint | Lateral malleolus | 44 | 1 3 |
| 18 | 54 | 7 days | Ruptured right biceps | Radial styloid process | 20 | 1 0 |

was reduced by skeletal traction under general anæsthesia Given 5 bottles of blood (2 0 litres) Red cell volume showed blood loss of 0 9 litre by the day after injury

**Case 5**—A boiler maker, aged 43, involved in a road accident, reached hospital four hours later A transverse fracture of a femur was treated by skeletal traction and reduction under general anæsthesia Local swelling was estimated to be 1 0 litre Given 2 bottles of blood (0 8 litre) Total blood-loss from red-cell volume on day after injury was 0 4 litre

**Case 6**—An engineer, aged 25, was involved in a road accident One and a half hours later he was pale, with B.P 145/95 mm Hg, pulse rate 106, and fractures of right femur (fig 1), lateral malleolus, and metacarpals Under general anæsthesia fractured femur was reduced by skeletal traction, and plaster was applied to the ankle Given 2 bottles of blood (0 8 litre) Blood loss from red cell volume on the day after injury was 1 6 litres

**Case 7**—A housewife, aged 62, knocked down by a car, sustained a comminuted fracture of the upper femur, bruising of both legs, and a fractured clavicle On admission she was pale and cold, with B P 110/70 mm Hg, pulse rate 80 Femur treated by skeletal traction Swelling at site of fracture was about 1 0 litre Total blood loss from red cell volume on day after injury was 1 9 litres

**Case 8**—An engineering worker, aged 63, struck in the back by a girder, sustained a fracture of iliac bone with moderate hæmatoma Swelling estimated at 0 8 litre Given 3 bottles of blood (1 2 litre) Blood loss from red-cell volume on day after injury 0 6 litre

**Case 9**—A man, aged 55, knocked off a bicycle, had a spiral fracture of the shaft of a femur, treated by traction Given a transfusion of 2 bottles of blood (0 8 litre) Blood loss from red cell volume on day after injury 1 7 litres

### *Differences in Limb Volumes*

These differences, estimated by serial circumferential measurements in 10 patients with closed injuries, are given in table II Associated injuries are ignored for this purpose The table gives the timing of the measurements and the distances over which they were made Tracings of radiographs of bony injuries are shown in fig 1 Case 18, not associated with any fracture, is shown in fig 2J Case 10 is of special interest because the swelling was measured with a high degree of accuracy in a limb with neither displacement nor instability of the fracture site

**Case 10**—A boy, aged 15, knocked off a bicycle, sustained an undisplaced fracture of the lower end of a femur *(fig 1)* The swelling was out of all proportion to the bony injury *The fracture was treated by skin traction and healed uneventfully* Limb swelling was found to be 1 2 litres Blood loss *determined by red cell volume on the day after injury was* 0 9 litre

Limb-volume differences estimated by the fluid displacement technique in 9 relatively minor injuries are shown in table III Tracings of the radiographs are shown in fig 1 and a photograph of case 10 in fig 2H

### *Hæmoglobin Levels*

Blood loss was estimated from the red cell volume in relatively few patients with closed fractures of the femur Of 9 such patients 3 showed a fall of Hb level to less than 12 5 g per 100 ml during the ensuing two weeks The estimated whole blood deficit in these cases (cases 1, 2, and 3) was 1 2, 1 3, and 2 0 litres None had received a blood transfusion The fall in Hb level often reflects the whole blood deficit at the end of emergency treatment

The Hb level was determined repeatedly *in 64 of 75 consecutive* cases of closed fracture of the femur *treated by one* team (excluding patients in the present series and patients with fractures confined to the femoral neck, trochanters, and condyles) Of the 64 patients 51 received no primary transfusion, and 31 of these showed a fall of Hb level to below 12 5 g per 100 ml

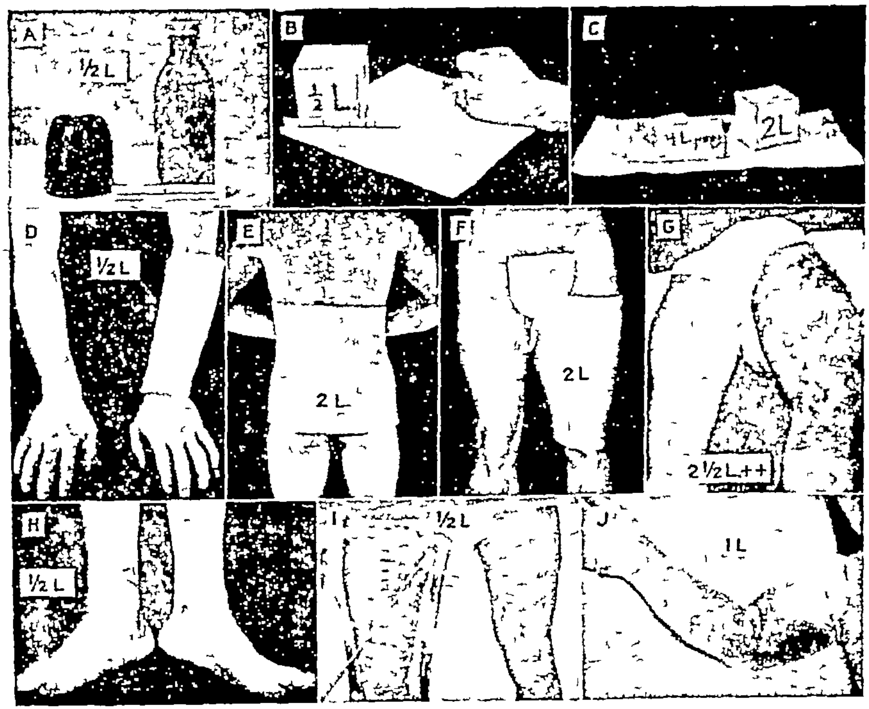

Fig 2—Swelling of soft tissues from blood loss A B C &c., see text.

during the two weeks after injury, and 16 of the 31 to below 11 0 g per 100 ml Only 4 showed no fall below 14·0 g per 100 ml. These observations show the frequency of mild anæmia following such fractures and suggest that the estimates of blood loss associated with closed fractures of the femur reported here are representative of the general run of injuries of this type

### *Photography and Reconstruction of Swelling*

The data given above have confirmed previous impressions that a valuable guide to blood loss is the volume of swelling at the site of injury We illustrate our approach by photography and by reconstruction of volumes in various clinically relevant forms (fig 2)

Fig 2A shows a bottle of blood beside half a litre of jelly, the volume of the contents of the bottle B shows a solid cube and a piece of surgical felt (the volume of each being that of half a litre of blood) alongside a fist, used as a rough guide by Grant and Reeve (1951) D shows a pair of normal forearms, one of which is wrapped in a half litre of felt, illustrating a degree of swelling not infrequently observed in fractures of the forearm, H (case 19, table III) shows half a litre of swelling from a fracture of the os calcis, and I shows half a litre of swelling from a fracture of the upper end of the femur (case 11, table II)

Fig 2C shows a cube and a piece of surgical felt each equal in volume to 2 litres of blood, compared with the half-litre cube and felt E shows 2 litres of felt wrapped round the back, representing the sort of swelling that can accompany fracture of the pelvis. Much larger swellings have been seen in patients with severe injuries to the trunk F shows the 2 litres of felt round the thigh representing a degree of swelling not infrequently seen in fractures of the femur G (case 34 table IV) shows gross swelling of the thigh associated with fracture of the shaft of the femur and amounting to more than 2 5 litres J (case 18 table II) shows 1 litre of swelling in the arm after rupture of the biceps muscle

### *Summary*

In summary the swelling associated with fractures of foot and ankle ranged from 0 15 to 0 50 litre with fractures of the tibia and fibula from 0 25 to 1 30 litres and with fractures of the shaft of the femur from 0·40 to 2 20 litres Red-cell volume showed whole-blood loss in similar fractures of the shaft of the femur to range from 0·40 to 1 70 litres

TABLE III—CLOSED FRACTURES LIMB VOLUME DIFFERENCES BY FLUID DISPLACEMENT

| Case no | Age (yr ) | Time after injury (hr ) | Site of fracture | Sites of measurement below tibial plateau (inches) | Volume differences (litre |
|---|---|---|---|---|---|
| 19 | 45 | 21 | Os calcis | 8 | 0 50 |
| 20 | 70 | 2 | Os calcis | 13 | 0 30 |
| 21 | 14 | 4½ | Lower tibial epiphysis | 0 | 0 30 |
| 22 | 46 | 6 | Ankle | 4 | 0 15 |
| 23 | 48 | 7½ | Ankle | 9 | 0 30 |
| 24 | 49 | 3 | Lower tibia | 9 | 0 25 |
| 25 | 62 | 1 | Ankle | 8 | 0 25 |
| 26 | 55 | 3 | Tibia and fibula | 1 | 0 45 |
| 27 | 46 | 22 | Tibia and fibula | 4 | 0·40 |

OPEN INJURIES

In open wounds and fractures measurement of blood loss is complicated by bleeding to the outside The extent of damage is often greater than in closed injuries and its assessment is more often complicated by further loss at operation associated with further trauma

The patients described below are typical of many major accidents The evidence for blood loss was obtained under conditions which allow early admission and early transfusion The degree of blood transfusion was greater than is common practice With smaller transfusions it would be hazardous to carry out many primary procedures which can now be completed with safety Blood transfusion was deliberately withheld from a few patients whose injuries would normally not be considered to require transfusion

In 12 male patients, aged 16–60 we attempted to assess the relative contribution of limb swelling blood loss to the exterior and further unexplained disappearance of whole blood With one exception (case 29) they claimed to be perfectly fit before the accident.

Patients were selected for inclusion in this series because (1) it was considered that they were likely to survive (2) veins were available, and the patient was sufficiently coöperative to enable the blood volume to be studied without interference with treatment or the creation of anxiety (3) the injuries were considered to be of sufficient severity for blood loss to be large enough to be measured by our methods and (4) they were free from

TABLE IV—OPEN INJURIES BLOOD LOSS CALCULATED FROM RED-CELL VOLUME COMPARED WITH CLINICAL ESTIMATE

| Case no | Age (yr ) | Site of open fracture | Visible damage to soft parts | Associated closed injuries | Follow up | | Day of r.c.v | A : whole blood deficit (litres) calculated from predicted normal by follow-up | | Lowest Hb level on day 4–14 (g per 100 ml.) | B blood transfusion (litres) | A + B whole-blood loss (litres) | | | C : clinical estimate | | (A + B) – C : remaining deficiency (litres) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Weight (kg ) | * Blood volume (litres) | | * (a) weight | (b) r.c.v by ³²P | | | (a) | (b) | Mean | Blood loss to outside (litres) | Limb swelling (litres) | |
| [illegible] | 43 | Tibia and fibula | + | | 50 | 4 4 | 1 | 1·0 | 0 1 | 12 3T | 0 | 1·0 | 0 1 | 0 6 | 0 1 | 0 5 | 0 |
| [illegible] | 49 | Femur | + | | 68 | 4 1 | 2 | 1 0 | 3 1 | 8 7 | 0 | 1 0 | 3 1 | 2 5 | 0 5 | 1 1 | 0·9 |
| [illegible] | 35 | Femur | + + | Clavicle | 73 | 5 5 | 2 | 1 [illegible] | 1 4 | 11 9T | 0 | 1 2 | 1 4 | 1 3 | 0 3 | 1·0 | 0 |
| [illegible] | 30 | Tibia and fibula | + | Dislocated hip | 70 | [illegible] | 2 | [illegible] 5 | [illegible] 0 | 10 3 | 0 | 2 5 | 2 0 | 2 2 | 0 4 | 1·0† | 0 8 |
| [illegible] | 60 | Femur | + + | | 66 | 4·0 | 2 | 0·0 | 1 0 | 9 9 | 2 4 | 3 0 | 3 4 | 3 2 | 1·0 | 1 5 | 0 7 |
| [illegible] | 16 | Tibia and fibula | + + + | Wrist | 57 | 4 3 | 1 | −0 8 | −0 3 | 13 7T | 3·6 | 2 8 | 3 3 | 3·0 | 2·0 | 0 7 | 0 3 |
| [illegible] | 21 | Tibia and fibula | + + + + | Femur | 43 | 3 [illegible] | 2 | 0 5 | −0 1 | 10·0 | 2 8 | 3 3 | 2 7 | 3·0 | 0 [illegible] | 2 5† | 0 3 |
| [illegible] | 48 | Tibia and fibula | + | Femur | 70 | 5 3 | 1 | 1 6 | [illegible] 5 | 9 3T | 3 8 | 5 [illegible] | 6 1 | 5 6 | 1 4 | 1·6† | 2·0 |
| [illegible] | 21 | Femur and foot | +<br>+ + | Knee | 61 | 4 0 | 2 | 1 7 | 1·2 | 10 4 | 4·0 | 5 7 | 5 2 | 5 1 | 2 8 | 2 5† | 0 1 |
| [illegible] | 22 | Patella and maxilla | + +<br>+ | Double femur and skull | 6[illegible] | 4 6 | 1 | 0 5 | −1 2 | 15 1 | 3·6 | 4 1 | 2 1 | 3 2 | 1·0 | [illegible]·0 | 0 2 |
| [illegible] | 38 | Humerus radius and ulna | + + + | | 54 | 4 0 | 1 | −2 3 | −2·0 | 16 1 | 4 3 | 2 5 | [illegible] 3 | [illegible] 6 | [illegible] | 1·0 | 1·0 |
| [illegible] | 2[illegible] | Skull (depressed) | + + | Ribs | 65 | 4 9 | 1 | −0 4 | −0 8 | 13 0 | [illegible] 1 | [illegible] 0 | 1 6 | 1 8 | 1 1 | 0 [illegible] | 0 5 |

+ ++ +++ ++++, for detailed interpretation see text.
r.c.v red-cell volume ³²P radioactive-phosphorus technique
T Hb level before blood transfusion for anæmia
* Predicted normal r.c.v = follow up weight (kg ) × 30 (ml ) and blood volume = weight (kg.) × 75 (ml.)
† Limb swelling determined by serial circumferential measurements

major visceral disturbances likely to interfere with the interpretation of evidence Each patient had at least one major fracture In table IV the extent and depth of the visible wound, irrespective of the associated fractures, are graded from + to ++++

+ represents the type of puncture wound often seen in a fracture “ compound from within ”, ++ represents a more severe wound involving skin damage or undermining of not more than one hand in area, with visible damage to structures beneath the level of the deep fascia, +++ represents a major wound with more extensive damage to skin, extensive undermining, and obvious severe damage to deep structures, and ++++ represents a degree of damage sufficient to warrant immediate primary amputation

Blood loss calculated from red cell volume was measured as described for closed injuries (table I) A shows the whole blood deficit or credit—i e, the difference between the measured red cell volume (day 1–3 after injury) and the “ predicted normal ” red cell volume derived from (a) follow up weight, and (b) follow up $^{32}$P red cell volume The lowest Hb level recorded during the ensuing two weeks is included as a further guide to whole blood credit or deficit B shows the blood transfused Whole blood loss (A + B) is calculated separately from follow up weight and $^{32}$P red cell volume and arbitrarily averaged

Such estimates of blood loss can be compared with the estimate (C) based on measurements of blood loss and limb swelling The difference between the blood-loss derived from these two approaches (*remaining deficiency*) is discussed in individual case histories

**Case 28**—A labourer, aged 43, was injured by a falling wall Twenty minutes later he was warm and pink, not sweating, with pulse rate 70, B P 150/95 mm Hg, a bruised loin, and fracture of the tibia and fibula open through a $^1/_4$ inch laceration Under general anæsthesia the fracture was fixed with wire, wound closed, and plaster applied Next day he developed atelectasis, and blood loss estimated from red cell volume was 1 0 litre from follow up weight but only 0 1 litre from follow up red cell volume The follow up red-cell volume remained unchanged twelve months later On clinical grounds there was probably some blood loss before admission At operation under tourniquet blood loss measured by swab weighing was 0 1 litre Blood loss into tissues and dressings was about 0 5 litre Blood loss of 0 1 litre based on follow up red cell volume is certainly an underestimate The Hb level fell from 15 5 g per 100 ml on admission to 13 6 g per 100 ml next day, and to 12 3 g per 100 ml the day after, suggesting an appreciable whole blood deficit He was given a transfusion of 1 6 litres After a period of polycythæmia his Hb level fell to 15 5 g per 100 ml This suggests that he lost less blood than the 1 6 litres transfused, and probably less than 1 0 litre

**Case 29**—A miner, aged 49, reached hospital four hours after a fall of coal on to his thigh His skin was warm and dry, ears pale, pulse rate 80, B P 115/80 mm Hg He had a comminuted fracture of the lower femur, open through a small wound Under general anæsthesia the wound was explored, cleaned, and sutured, and the fracture fixed in a Thomas's splint He gave a history of partial gastrectomy for ulcer a year previously, from which he had not fully recovered Two days after injury blood loss calculated from red cell volume was 1 9 litres by follow up weight and 3 1 litres by follow up red cell volume On admission and for some weeks afterwards he had a sallow complexion, anxious facies, and low serum protein and serum iron levels On discharge he thought he looked better and had put on weight Blood loss estimated from follow up red cell volume is probably excessive because he was probably both anæmic and oligæmic before injury Blood-loss into a polythene bag and by swab weighing at operation was 0 5 litre Limb swelling was 1 1 litres, suggesting a total blood loss of 1 5–2 0 litres The remaining deficiency can be accounted for by anæmia before admission His Hb level fell from 12 3 g per 100 ml on admission to 8 7 g per 100 ml eight days later, averaging 14 2 g per 100 ml from follow up studies The evidence suggests blood loss of 1 5–2 0 litres by the second day

**Case 30**—A man, aged 35, involved in a motor-cycle accident, reached hospital twenty five minutes later, with fractures of clavicle and shaft of femur, the latter open through a contaminated laceration Under general anæsthesia d was cleaned, explored, and closed, and the fracture reduced and fixed in a Thomas's splint His general condition remained excellent for three days He then developed pain and swelling from infection of the fracture hæmatoma For a time it seemed that the limb would be lost, but eventually infection was controlled He was left with a stiff but painless knee Two days after injury blood loss calculated from red cell volume was 1 4 litres from follow up red cell volume and 1 2 litres from follow up weight, average 1 3 litres Primary limb swelling was estimated to be less than 1 0 litre Blood loss at operation by swab weighing was 0 3 litre The lowest Hb level on the fourth day after injury was 11 9 g per 100 ml The evidence suggests whole blood loss of about 1 3 litres during the first two days

**Case 31**—A painter, aged 30, was involved in a road accident Two and a half hours after injury his skin was pale and cold, B P 125/80 mm Hg, pulse regular, good volume, rate 80 He had a fracture of the left tibia and fibula open at a small wound The left hip was dislocated, the leg was tensely swollen, foot cold At operation the hip was reduced, the leg wound excised, explored, and sutured, and the fracture reduced and put in plaster Later a bruise of the shoulder was found Two days after injury blood loss calculated from red cell volume was 2 0 litres Blood loss from the wound by swab weighing was 0 4 litre, measured swelling of the leg was 1 0 litre The remaining deficiency of 0 8 litre could be explained by extravasation at the site of his hip and shoulder injuries Hb level fell to 10 3 g per 100 ml on the seventh day The evidence suggests a primary blood loss of about 2 0 litres

**Case 32**—An engineer, aged 60, was knocked off his bicycle Two hours after injury he was found to have an open comminuted fracture of the lower femur He was conscious and pale, neither restless nor sweating, with nose and forehead warm, pulse and B P normal Under general anæsthesia the wound was cleaned and sutured and the fracture reduced and splinted. He was transfused with 2 4 litres of blood The wound healed uneventfully Two days after injury blood loss from red cell volume studies was (a) 3 0 litres, and (b) 3 4 litres, mean 3 2 litres Before and during operation external blood loss was estimated at 1 0 litre and limb swelling 1 5 litres The remaining deficiency of 0 7 litre could be due to blood loss to the outside before admission Hb level was 13 0 g per 100 ml on the day after admission and fell to 9 9 g per 100 ml on the eleventh day Taken as a whole the evidence suggests primary blood loss of about 3 0 litres

**Case 33**—A boy, aged 16, was involved in a motor cycle accident Forty minutes later he was pale, not sweating, with extremities cold, face warm, pulse rate 72, B P 85/55 mm Hg, rising to 110/75 mm Hg within an hour He had fractures of the wrist and foot and a severe open fracture of the middle of the leg Under general anæsthesia one and a half hours after injury the leg was amputated at the fracture site He received 9 bottles (3 6 litres) of blood His postoperative condition was excellent On the day after injury and transfusion whole blood loss from red cell volume studies was (a) 2 8 litres and (b) 3 3 litres, mean 3 0 litres Blood loss at operation by swab weighing was 2 0 litres, and swelling of the limb 0 7 litre Hb level fell from 16 5 g per 100 ml on admission to 13 7 g per 100 ml on the seventh day, Total blood loss was about 3 0 litres or more

**Case 14**—A polisher, aged 21, was involved in a road collision An hour and a half later he was pale and cold He had a double closed fracture of the femur with a large hæmatoma, fractured tibia and fibula, with extensive skin and muscular damage His pulse was regular, volume poor, B P 110/70 mm Hg After 1 bottle of blood the B.P rose to 150/80 mm Hg Three hours after admission the leg was amputated through the fracture site, and the fractured femur treated by traction, under general anæsthesia Two days after injury and transfusion of 2 8 litres of blood, whole-blood loss from red cell volume studies was estimated as (a) 3 3 litres and (b) 2 7 litres, mean 3 0 litres Blood loss before and during operation was found to be 0 6 litre Swelling of the thigh was about 2 0–2 5 litres A small remaining deficit could be explained by bleeding before admission and further bleeding into the tissues and dressings after operation Hb level fell to 10 g per 100 ml two days later The evidence suggests blood loss of at least 3 0 litres and possibly more.

**Case 12**—A foreman, aged 48, was involved in a motor cycle accident Fifteen minutes later his skin was pale and warm, pulse-rate 85 B.P 150/85 mm Hg He had a double closed fracture of the shaft of the femur and an open fracture of the same leg Bleeding from the open fracture had soaked the leg of his trousers. At operation two hours later the leg wound was explored and the fracture plated. A laceration of the other leg was sutured and the fracture of the femur treated by skeletal traction. He received 9 bottles (3·6 litres) of blood; his postoperative condition was excellent. Two days after injury he became irrational developed a rash and was dyspnœic Fat-embolism was diagnosed During the following week he improved steadily but recovery was complicated by sloughing of the skin over the leg fracture On the day after injury and transfusion whole-blood loss calculated from red-cell volume was (a) 5·2 litres and (b) 6·1 litres mean 5·6 litres Blood loss before and during operation was estimated at 1·4 litres including 1·1 litres measured by swab weighing swelling of the thigh was 1·0 litres. The remaining deficit might be due to (1) blood loss before admission, (2) extravasation into the leg and (3) blood disappearance associated with the processes later diagnosed as fat-embolism. Hb level fell to 9·3 g per 100 ml on the fourth day when another transfusion was given. The evidence suggests considerable whole blood deficit at the end of emergency treatment in spite of a large transfusion with total blood loss of more than half his blood volume

Case 34 —A carpenter, aged 31 struck on the leg by a crane, was admitted to hospital forty minutes later cold and pale with B.P 110/80 mm. Hg pulse rate 110 He had a deep laceration of the foot and enormous swelling of the left thigh, with an anterior puncture wound, and transverse fracture of the femur with wide separation Under general anæsthesia a complete tear of ligamentous structures on the medial side of the knee was found At operation the femur was fixed with a Küntscher nail. The exploration allowed evacuation of a hæmatoma and closure of the deep muscles. The laceration of the foot was cleaned and sutured On return to the ward after transfusion of 9 bottles (3·6 litres) of blood the extremities were cold and his blood pressure had fallen After 1 more bottle (0·4 litre) his condition improved. He improved steadily thereafter On the day after admission blood loss from red cell volume studies was (a) 5·7 litres and (b) 5·2 litres, mean 5·4 litres. The limb swelling was great; serial circumferential measurements suggested an increase in volume of 2·5 litres or more Blood loss to the outside was about 2·8 litres including 1·8 litres measured by swab-weighing Hb level fell to 10·4 g per 100 ml. on the eleventh day Taken as a whole the evidence suggests a total blood loss of about 5·5 litres.

Case 35.—A man aged 33 involved in a motor-cycle accident arrived at hospital three hours after injury conscious but lethargic with skin pale and cold B.P 180/70 mm Hg pulse-rate 50 He had a severe fracture of the skull fractures of the mandible lacerations of the chin, fractures of the right radius and 1st and 2nd metacarpals, bilateral closed fractures of the shaft of the femur and an open fracture of the patella. Transfusion was started and continued overnight. Next morning the knee wound was cleaned and sutured and the patella excised The mandible was wired, the malar bone raised, the wrist put in plaster after manipulation and the lacerations sutured. The pulse-rate remained slow—50–60—for some hours after admission. Subsequently he was proved to have an intracranial lesion which left him permanently blind. He proceeded to make an otherwise satisfactory recovery On the day after admission after transfusion of 9 bottles (3·6 litres) of blood, whole blood loss calculated from red-cell volume studies was (a) 4·1 litres and (b) 2·4 litres, mean 3·2 litres Follow up $^{32}$P red-cell volume was estimated in this patient when he was confined to bed and could not be weighed. He was not weighed until some months later Probably the whole blood loss estimated at 4·1 litres is more accurate than that based on early follow up red-cell volume The known swellings could account for 2·0–2·5 litres. He probably lost something like 1·0 litre of blood to the outside If the blood loss calculated from red-cell volume is taken as 4·1 litres, the remaining deficit could be accounted for by oozing into dressings and underestimate of limb swelling. The Hb level showed no significant fall this suggests that blood loss was satisfactorily replaced by transfusion. The total evidence therefore suggests a blood loss of 3·5 litres.

Case 36 —A house-painter aged 20 was involved in a rail smash. Two hours later he was pale and restless with cold extremities B.P 105/60 mm. Hg pulse rate 80 He was mildly concussed with extensive injury to the right arm multiple fractures of humerus radius, and ulna partial dislocation of the elbow and damage to skin and muscles Surgery was delayed for observation of his cerebral state Blood transfusion was continued through the night and during a two hour operation next morning Considerable bleeding took place before and during operation at which the humerus was plated and the wound was cleaned and closed by suture and skin grafting He received 12 bottles (4·8 litres) of blood Next day whole blood loss from red-cell volume studies was (a) 2·5 litres and (b) 2·8 litres mean 2·6 litres. The limb swelling probably amounted to 1·0 litre leaving a remaining deficiency of 1·6 litres, which could be explained by bleeding before and during operation This case emphasises the difficulty of assessing blood loss at operation without swab-weighing Hb level did not fall below 17·1 g per 100 ml during the two weeks after trauma The follow up value was 15·0 g per 100 ml This supports our red cell evidence that he received more blood than he had lost The evidence suggests blood loss of about 2·5 litres.

Case 37 —A fitter's mate aged 25 fell down a lift shaft and sustained an open depressed fracture of the skull with no brain damage Half an hour after injury the B.P was 128/80 mm. Hg and pulse rate 80 Radiographs showed fractures of ribs 8 9 and 10 After a period of observation the fractured skull was explored bone was removed, and the wound was closed. He left hospital after sixteen days On the day following injury, after transfusion of 6 bottles (2·4 litres) of blood, blood loss calculated from red-cell volume was (a) 2·0 litres and (b) 1·6 litres mean 1·8 litres Blood loss by swab-weighing at operation was 1·1 litres, swelling at the site of the head injury was not more than 0·2 litre The remaining deficit of 0·5 litre could be explained by bleeding into other sites of injury and before admission and oozing into the dressings. Hb level fell from 14·9 g per 100 ml on admission to 13·0 g per 100 ml. on the ninth day The evidence suggests blood loss of about 2·0 litres.

In most of the patients described above the total blood loss can be explained by limb swelling plus blood loss to the outside, the remaining deficit being less than the error of the methods involved (probably ±1·0 litre) In 2 out of 12 patients (cases 12 and 30) the remaining deficit was more than 1·0 litre The contribution of blood loss into limb swelling appeared in many instances to be appreciable The contribution of blood loss to the outside varied from 10 to 90% of the total loss In the three patients (cases 33 36 and 37) in whom blood loss to the outside exceeded 50% of the total blood loss a large proportion of this occurred at operation and was measured by swab weighing in cases 33 and 37 Of the remaining 9 patients 6 showed blood loss to the outside varying only between 10% and 25% of the total blood loss This suggests that blood loss to the surface in many open fractures is often less important than blood loss into the tissues except where major blood loss occurs during an operation

Data are presented in table V on 12 other patients in whom estimates of blood loss were based chiefly on blood volume measurements The table includes 3 cases (cases 38 39 and 46) where blood was lost to the outside only during the operation; it also includes the nature of the injury and of the primary surgery

Two of these patients received abdominal injuries associated with fractures of the pelvis Case 38 sustained a major rupture of the liver with a central dislocation of the hip At operation blood loss to the outside measured by swab weighing was 0·8 litre. He received 3·6 litres of blood Total blood loss was estimated to be 5·0 litres on the tenth day after injury At this time there had been further bleeding in association with the withdrawal of a pack used to stop hæmorrhage from the liver Case 39 sustained a severe fracture of the pelvis and a tear of the omentum, which was sutured at laparotomy He received 2·5 litres of blood Total blood loss was estimated at 3·0 litres.

Cases 40 and 41 are examples of severe injury where amputation was only decided on after review of the extent of damage Exploration was done in the presence of suspected vascular injury without a tourniquet; considerable blood loss took place during exploration In each case a transfusion of 4 0 litres enabled this to be done safely It was insufficient to prevent a post traumatic whole blood deficit of 0 9 and 1 4 litres respectively.

In cases **42–46** blood transfusions of 2 4, 5 2, 1 6, 2 8, and 2 4 litres were given, allowing major operations to be done in the acute phase of injury Surgery added to loss of blood but did not increase the risk to life Three of these patients received transfusions which exceeded blood loss and were none the worse for it They did not develop post traumatic anæmia Case 42 was left with a whole blood deficit of 0 6 litre, and case 46 0 7 litre, the lowest Hb levels being 14 4 g and 12 0 g per 100 ml respectively

**Cases 47 and 48** had multiple injuries requiring surgery as indicated in table v Case 47 received 2 4 litres of blood and was left on the third day with a whole-blood deficit of 1 4 litres, suggesting total blood loss of 3 8 litres The Hb level fell to 9 9 g per 100 ml during the ensuing two weeks Case 48 received 2 8 litres of blood Blood volume on the third day suggested a deficit of 0 5 litre and total blood loss of 3 3 litres His Hb level fell to 9 8 g per 100 ml during the post-traumatic period

**Case 49** had extensive undermining of the skin, eventually leading to full thickness loss over two thirds of the leg (7% of the body surface) A primary transfusion of 3 2 litres of blood was sufficient to tide her over partial excision and suture without any immediate post-traumatic oligæmia or anæmia The estimated blood loss was 2 9 litres

The 24 cases presented in tables IV and V illustrate some of the factors influencing total blood loss in some complex open and closed civilian injuries The extent of damage to soft tissues is only a partial guide to blood loss Usually the bigger the wound the less measurable is the blood-loss, and the more complex the total damage the more unpredictable is the total blood-loss

Surgery can decrease blood-loss by direct control of bleeding, removal of damaged tissues, and obliteration of dead space , it can also increase both blood loss and tissue damage even where every effort is made to reduce the latter to a minimum At times it is necessary to operate on a limb without a tourniquet, and then blood loss can be considerable (case 36) With a tourniquet blood loss at operation may be minimal (case 28)

Blood-transfusion may increase blood-loss , therefore it is impossible to say how much of the blood loss recorded would have occurred with less transfusion or none at all In view of the possible argument that we have misleadingly increased blood-loss by transfusion, cases 28–31 were selected as patients from whom it was clinically justifiable to withhold transfusion

Some injuries with direct arterial damage, or in areas such as the face and scalp, may bleed out of all proportion to the size of the wound Usually, however, there appears to be some correlation between over-all blood loss in

TABLE V—BLOOD-LOSS FROM RED-CELL VOLUME

| Case no | Age (yr ) | Nature of injury | Visible damage to soft parts | Diagnosis | Surgery | Follow up | | Whole blood deficit on day of R.C V | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | Weight or height | Blood volume (litres)* | Day of R.C V | Method of calculating R C V | A Whole blood deficit (litres) calculated from predicted normal* by follow up | Lowest Hb level on day 4–14 (g per 100 ml ) | B blood transfusion (litres) | A + B whole blood loss (litres) |
| 38 | 48 | Road accident | | Ruptured liver , concussion , central dislocation of hip | Laparotomy, packing, and extension | 87 kg | 6 5 | 10 | $^{32}$P R C V | 1 4 | 13 3 | 3 6 | 5 0 |
| 39 | 15 | Caught in ash-conveyor | | Fractured pelvis , omental tear | Laparotomy | | 4 7 | 2 | P V + H'crit | 0 5 | 14 9 | 2 5 | 3 0 |
| 40 | 30 | Road accident | + + + + | Open fracture of tibia and fibula into knee | Amputation | 166 cm $^1$ | 4 5 | 3 | P V + H crit | 0 9 | 12 6 | 4·0 | 4 9 |
| 41 | 45 | Crushed in machine | + + + + | Severe destruction of upper limb | Amputation of upper arm | 69 kg | 5 2 | 1 | $^{32}$P R C V | 1 4 | 13 8 | 4 0 | 5 4 |
| 42 | 57 | Hit by tub of stone dust | + + | Open fracture of tibia and fibula | Plating and rotation—flap | 85 kg | 6 4 | 5 | I V + H crit | 0 6 | 14 4 | 2 4 | 3 0 |
| 43 | 55 | Caught in rolling-machine | + + + | Major lacerations of both hands | Toilet, suture, and grafting | 65 kg | 4 9 | 10 | $^{32}$P R C V | −0 9 | 16 6 | 5 2 | 4 3 |
| 44 | 38 | Hit by pillar | + + | Lacerated scalp , severe fracture of femur | Suture and extension | 65 kg | 4 9 | 8 | P V + H crit | −0 6 | 15 3 | 1 6 | 1 0 |
| 45 | 26 | Road accident | | Fractured 6 ribs , fracture dislocation of thoracic spine | Open reduction and wiring of spine | 51 kg | 3 8 | 5 | P V + H'crit | −1 5 | 17 3 | 2 8 | 1 3 |
| 46 | 25 | Crushed by tractor | + + | Severe open fracture of femur | Toilet plating, and suture | 72 kg | 5 4 | 1 | P V + H'crit | 0 7 | 12 0 | 2 4 | 3 1 |
| 47 | 27 | Hit by railway engine | + + + | Gross injury to hand , open depressed fracture of skull fractured humerus, tibia and fibula, and os calcis | Suture, exploration and elevation, plaster spike reduction of os calcis | 68 kg | 5 1 | 3 | P V + H crit | 1 4 | 9 9 | 2 4 | 3 8 |
| 48 | 54 | Road accident | + + + | Concussion , lacerated scalp, open fracture of left tibia and fibular , closed fracture of right tibia and fibula | Exploration, plating and plaster | 57 kg | 4 3 | 3 | P V + H'crit | 0 5 | 9 8 | 2 8 | 3 3 |
| 49 | 60 | Run over by bus | + + + | Destruction of $^2/_3$ of skin of thigh and leg | Toilet, excision suture and graft | 156 cm $^2$ | 3 4 | 11 | P V + H'crit | −0 3 | 15 1 | 3 2 | 2 9 |

+, + +, + + +, + + + +, for detailed interpretation see text R C V , red cell volume
$^{32}$P radioactive phosphorus technique P V , plasma volume

*Predicted normal R.C V = follow up weight (kg ) × 30 (ml.) and blood volume = weight (kg ) × 75 (ml ) with the following exceptions . 1 based on height because of amputation figures of Gibson and Evans (1937) used with no allowance for lost limb 2, female, figures of Gibson and Evans (1937) used.

open injuries with major fractures and the size and extent of the wound. Large wounds with total transection of deep structures, including main vessels may appear to bleed little, but their total blood loss is nevertheless great (case 41). We have found that when amputation has been necessary at the acute stage through the arm, thigh, or leg, blood loss is rarely less than 2·0–2·5 litres and often more (cases 33, 40 and 41), some of this may be due to extravasation into the stump after operation.

Blood loss after the end of emergency treatment was rarely sufficient to alter the clinical picture. Frank hæmorrhage may come on during dressing or removal of a deep pack (case 38). Disappearance of red cells may accompany infection (case 30) or fat-embolism (case 12). Patients with severe injuries of the skin and subcutaneous tissue with gross undermining may lose large amounts of blood in the absence of bony or gross muscular damage (case 40).

In such injuries it is impossible to summarise all the factors which contribute to the extent of blood loss, but some of them are indicated above.

### Discussion and Conclusions

We have attempted to assess blood loss associated with various civilian injuries. Apart from direct measurement of bleeding from the wound, all our methods are indirect and give information that could be regarded as somewhat inconclusive. The accumulation of evidence from different approaches convinced us that all these methods contribute to a better quantitative understanding of primary blood loss associated with trauma. In closed injuries of the limbs we can roughly estimate the degree of blood loss from the size of the primary swelling. Such assessment is made more easily in moderate and more peripheral injuries. The general accuracy of this approach is confirmed by studies of red-cell volume and hæmoglobin level.

Many closed fractures and injuries to soft parts are associated with blood loss of about 0·25–0·50 litre (less than 10% of the total blood volume). They correspond to Grant's "wounds of less than one hand." Patients with such lesions do not require transfusion and from the point of view of blood loss, such lesions are not in themselves relevant to "traumatic shock" or "the illness of trauma." Typical examples are the common fractures of the ankle, knee, and forearm. In multiple injuries each of such injuries can contribute its quota to the total blood loss.

We made detailed observations on closed injuries corresponding in their degree of blood loss to the "moderate wounds" of Grant and Reeve (1951). This group is represented by the average fracture of the shaft of the femur, by some fractures of the tibia and fibula, and by major fractures of the upper limb. Some injuries to the trunk come into this category but are more difficult to assess. Such injuries lose about 0·5–1·5 litres of blood (10–30% of the total blood volume).

Multiple fractures may be associated with much greater blood loss. On occasions a single injury to the thigh may be associated with blood loss of 2·0–2·5 litres or even more. Fractures of the pelvis even without major visceral damage, can lose even larger quantities of blood. Such injuries correspond to the "large" and "very large wounds" of Grant and Reeve (1951) and can lose 40–50% or more of the total blood volume.

Severe multiple injuries however are rarely completely closed, and some of the lesions are almost invariably associated with blood loss to the exterior.

Blood loss in many open fractures results from bleeding into the tissues and to the outside in variable proportions. Most of the patients studied in this series would from the extent of total blood loss, come into the category of "large" and "very large wounds" (Grant and Reeve 1951). Such categorisation is only partly valid, because our assessments include blood loss at operation during the emergency phase. Without surgery some patients would have bled less and some more. In practice the distinction is not of great importance where surgery is absolutely indicated.

The extent of blood loss in open injuries will depend moreover not only on the extent of injury but also on its treatment and on the timing of such treatment. Assessment must depend on consideration of the dynamic interplay of several individual factors. In many patients with severe or multiple injuries estimation of blood loss to a degree of accuracy necessary for the control of transfusion may only be possible by blood volume studies.*

We did not find it necessary to introduce the suggestion of Grant and Reeve (1951) that a large unexplained disappearance of red cells may take place during the first two days after injury. The crudeness of our assessments makes it impossible to exclude a small unexplained disappearance of red cells, but in the injuries which we investigated such unexplained loss probably did not exceed 10% of the red-cell volume and was of little clinical importance compared with bleeding.

Useful guides to the amount of blood lost from local injuries are the volume of swelling and that of blood loss to the outside. Often such information can be more important, particularly in the prevention of "shock," than assessment of blood loss from the patient's clinical state as a whole.

Whatever attitude is adopted towards transfusion, those concerned with treating injuries in the acute phase must ask themselves certain questions: how much blood has been lost, and when, and where? How much blood is likely to be lost after admission, during operation, and postoperatively? What effects are likely to result if the blood is inadequately replaced? How do the risks involved in transfusion in the particular circumstances of the particular hospital compare with the risks of neglecting the effects of oligæmia and anæmia?

The amount of blood lost in various injuries is greater than is usually recognised but can often be diagnosed or predicted by study of the local injuries even in the absence of clinical signs of "oligæmic shock."

### Summary

Blood loss was studied in 40 injured patients.

Blood loss from 10 closed limb injuries was calculated from red cell volume studies.

Blood loss from 10 closed limb injuries was estimated by comparison of the volumes of injured and normal limbs.

Blood loss from 12 open injuries was estimated by (*a*) red-cell volume studies, (*b*) hæmoglobin studies, and (*c*) *estimation of blood loss in limb swelling and to the outside.*

Further evidence of the amount of blood lost in various injuries is based on blood volume studies on 12 patients.

Further evidence of blood loss in closed injuries is derived from hæmoglobin studies on 75 patients (additional to the above) with fractures of the shaft of the femur.

An attempt is made to record photographically the appearance of various volumes of swelling.

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* Since this paper was written Prentice et al. (1954) have published an important study of blood volume and blood transfusion therapy based on experience gained in the Korean war. If account is taken of the very serious nature of many of the injuries studied by them, their observations clearly bear a close relationship to our observations on less severe civilian injuries. They attribute the discrepancies between the large amounts of blood given and the small blood volumes determined subsequently to bleeding "either externally or into the tissues during the preoperative, operative and postoperative periods."

This evidence is used to define the amount of blood-loss associated with various injuries, with particular emphasis on the contribution of limb swelling

It is suggested that quantitative assessments based on such methods can provide a guide to the need for blood-transfusion

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# TREATMENT OF PULMONARY SARCOIDOSIS WITH STREPTOMYCIN AND CORTISONE

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WHEN effective chemotherapy for tuberculosis was discovered, it was logical to try this in sarcoidosis because the two maladies may be related Later, when cortisone became available, we used it together with streptomycin and *p* aminosalicylate (P A S) because of its action in controlling productive inflammation We describe here their effects on 38 selected patients with pulmonary sarcoidosis

## Methods and Material

A strictly controlled therapeutic trial was impracticable because so few patients were available We chose the alternative of watching the course of the disease in each patient, before treatment, for long enough to establish an unfavourable trend and then observing the effect of treatment on subsequent progress

The diagnosis of sarcoidosis was based primarily upon the radiological changes in the lungs When the disease was recent, the hilar lymph nodes were usually enlarged and the lungs showed either numerous symmetrical miliary opacities (fig 1*a*) or fewer and larger opacities up to a few centimetres in diameter (fig 2*a*) Older disease showed as fine reticulation or coarse linear or massive shadows, often with distortion of the hilum by severe fibrosis (fig 3*a*) No case with enlarged hilar lymph nodes alone was treated 8 patients with pulmonary lesions also had uveitis, 4 severely All the patients had at least two sputum or gastric lavage cultures set up before treatment, none grew *Mycobacterium tuberculosis* Tuberculin sensitivity was usually low or absent Epithelioid cell follicles, typical of sarcoidosis, were found at biopsy in 36 patients in liver (30), lymph nodes (6), skin (5), lungs (2), and conjunctiva (1)

### *Streptomycin Series*

30 patients were treated with streptomycin sulphate and sodium P A S There were 11 males and 19 females, aged 13-63 With 4 exceptions the disease had been present for at least six months, and in 11 for more than two years, without showing spontaneous improvement The onset was dated from the first definite symptom—e g, iritis and erythema nodosum—or from the first abnormal radiograph, so the date is only approximate Pulmonary symptoms were at first so slight that they were an unreliable guide to the duration of the disease

Streptomycin was given intramuscularly in doses of 1 g daily 7 patients were treated for six to eight weeks, 13 for three months, and 10 for six to twelve months 7 of these latter patients received streptomycin only twice or thrice weekly All the patients also received at least 12 g of P A S daily

### *Cortisone Series*

20 patients were treated with cortisone acetate, streptomycin, and P.A S, including 12 who had not responded to streptomycin and P A S There were 3 males and 17 females, aged 19-63 9 were treated for two months, and the rest for four months to a year At first we used cortisone when the disease was severe or long standing and had a bad prognosis Later we treated less advanced cases Cortisone was given in doses of 150 mg orally each day for two months, and in doses of 75-100 mg subsequently to those who continued treatment All the patients were also given streptomycin 1 g each day or twice weekly with calcium P.A.S The consumption of salt was restricted, and a close watch was kept for side effects, in particular the weight and blood pressure were recorded regularly and the urine was tested for sugar Our early cases were treated at rest in hospital, but later we allowed ambulant treatment at home with supervision at a special clinic Patients were encouraged to do light work when they were fit enough

### *Assessment of Results*

The effects of treatment were judged mainly by chest radiographs and by serial liver biopsies The degree of radiological improvement was graded as slight or moderate when the opacities diminished by less than 50%, and great when they diminished by more than this Pulmonary symptoms and signs were variable even before treatment was given and were therefore unreliable guides to progress The function of the lungs was studied before and during, or at the end of, treatment in 4 patients given streptomycin and P A S and in 7 given cortisone The factors tested were maximal breathing capacity, ventilation at rest, lung volumes, and mixing efficiency estimated with a helium oxygen mixture

The results of treatment were analysed in relation to the estimated duration of the disease The rate and extent of radiological improvement in the patients with pulmonary sarcoidosis treated with streptomycin were compared with those of 12 patients with pulmonary tuberculosis treated in the same way All the latter had widespread pulmonary infiltration, and tubercle bacilli in the sputum they were 7 males and 5 females, aged 18-52

## Results

### *Streptomycin*

30 patients with pulmonary sarcoidosis were treated with streptomycin and P A S (table I) Judged radiologically 12 were unchanged and 12 improved 6 others also improved, but since this improvement was not closely related to the period of treatment it was regarded as spontaneous The remaining 24 patients were analysed in two groups

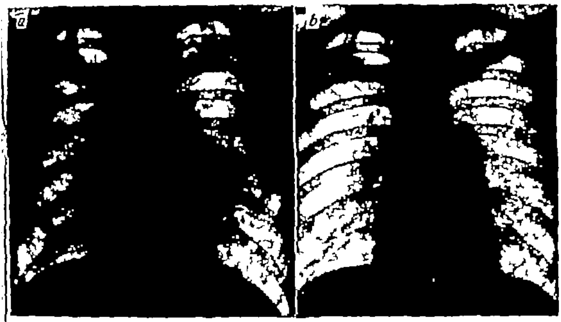

Fig 1—Pulmonary sarcoidosis in a man aged 25: a before treatment and a year after onset; b after two months' treatment with streptomycin

Liver biopsy showed sarcoid follicles. Despite increasing infiltration for one year there was complete radiological clearing after three months' treatment.

Group I comprised 9 patients with disease of at least two years' duration, the average being three and a half years; nearly all of them had conspicuous dyspnœa and either confluent or linear opacities, or both, in the chest radiograph (fig 3a). Group II comprised 15 patients whose disease had been present for less than two years.

Only 1 patient out of 9 in group I showed any radiographic improvement; in group II 11 out of 15 improved, 8 of these greatly, 3 of them completely. Typical appearances before and after treatment are shown in fig 1. 5 patients had uveitis; in 2 the inflammation subsided during treatment; the others were not improved.

The duration of the disease before treatment, the time of onset and the duration of radiographic clearing in each patient who improved were compared with those of the 12 patients with pulmonary tuberculosis treated in the same way (fig 4). Improvement usually began after one to three months, and in this respect and in the time taken for maximal improvement the patients with sarcoidosis resembled those with pulmonary tuberculosis.

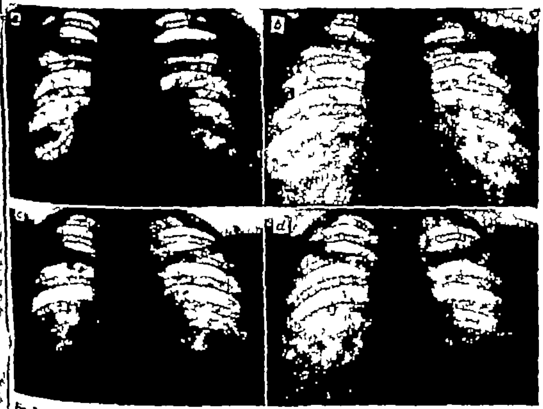

Fig 2—Pulmonary sarcoidosis in a girl aged 18: a before treatment; b after two months' treatment with cortisone and streptomycin; c relapse four months after treatment; d after a year's further treatment.

She had general ill health, an enlarged spleen and increasing pulmonary infiltration for two years, all of which responded to treatment.

Only 1 patient of those who were breathless benefited in this respect after treatment, and this happened although the disease was advanced. There was, however, no corresponding change radiographically or in the physiological tests. Three others with mild dyspnœa on exertion and slightly abnormal breathing tests were unchanged, judged either clinically or by laboratory tests, although the radiographic change was striking.

Serial biopsies were done in 9 of the patients with sarcoidosis who had follicles in the liver before treatment. After treatment the liver was normal in 2; the follicles were smaller and somewhat more fibrous in 2, and fewer but larger in 3. The remaining 2 who did not improve radiographically did not show any histological change. All these features, including increase in size of the follicles, have been found also during natural healing (Mather, Dawson, and Hoyle unpublished).

The 12 patients who improved during treatment with streptomycin and P.A.S. were followed for from one and a half to five years. 3 who had shown only slight radiographic clearing have relapsed. 2 of these had had their disease for at least eighteen months before treatment, and all 3 were treated early in the series for three months only. The remaining 9 are well and have not deteriorated.

TABLE I—RADIOLOGICAL ASSESSMENT OF RESULTS OF TREATMENT OF PULMONARY SARCOIDOSIS WITH STREPTOMYCIN AND P.A.S.

| Duration of disease (yr.) | No. treated | No change | Improvement | Improvement unrelated to treatment |
|---|---|---|---|---|
| More than 2 | 9 | 8 | 1 | 0 |
| Less than 2 | 21 | 4 | 11 | 6 |
| Total | 30 | 12 | 12 | 6 |

## *Cortisone and Streptomycin*

20 patients were treated with cortisone, streptomycin, and P.A.S. The results were analysed in the same way as the results of antibacterial therapy alone (table II). 11 patients whose disease had been present for more than two years (group I) were treated. 8 of them had already not responded to streptomycin with P.A.S. All were dyspnœic before treatment, 6 severely; only 2 were less short of breath afterwards. 2 patients had splenomegaly, which diminished. 8 of the 11 in this group improved to some extent radiographically, although appearances suggested that they had extensive fibrosis and emphysema. Fig. 3 illustrates a typical example.

In group II, where the disease had been present for less than two years, the results of treatment were much better than in group I. The pulmonary infiltration improved in all 9 patients, greatly in 5. Moreover, the improvement was more rapid than after antibacterial treatment alone; it began in about two weeks and reached a peak in four to six weeks. Fig. 5 shows an example. Only 2 patients in this group were dyspnœic, but neither got relief

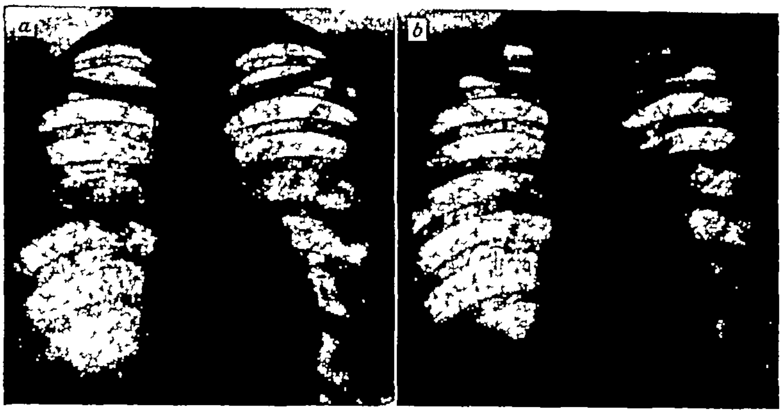

Fig 3—Pulmonary sarcoidosis in a woman aged 30 *a*, before treatment and seven years after onset , *b*, after two months' treatment with cortisone and streptomycin

She had progressive dyspnœa and an enlarged spleen, and liver biopsy showed sarcoid follicles

Although nearly all the patients who received cortisone had their most serious lesions in the lungs, a few had important changes elsewhere 4 had uveitis, 2 severely, which cleared completely during treatment One of these had a granulomatous conjunctivitis and cutaneous sarcoids as well, which healed but left slight scarring Another had, in addition to the uveitis, hypercalcæmia with evidence of renal damage and generalised lymph-node enlargement , all these features responded well to treatment Of the 4 patients with uveal tract sarcoidosis 2 have maintained their improvement two and six months after stopping cortisone, but 2 have required prolonged treatment

The function of the lungs was studied before and during treatment in 7 patients 5 of these were severely breathless , in 3 neither symptoms nor lung function improved, although there was some radiographic clearing in 1 of them The 2 others, whose radiographs showed moderate clearing, were less short of breath , 1 of these had an increased maximal breathing capacity and a reduced residual air-space, due to relief of bronchospasm , the other showed no change in the tests The 2 patients who were only slightly breathless had little abnormality in lung-function tests and were unimproved by treatment in these respects, although there was a good radiographic response

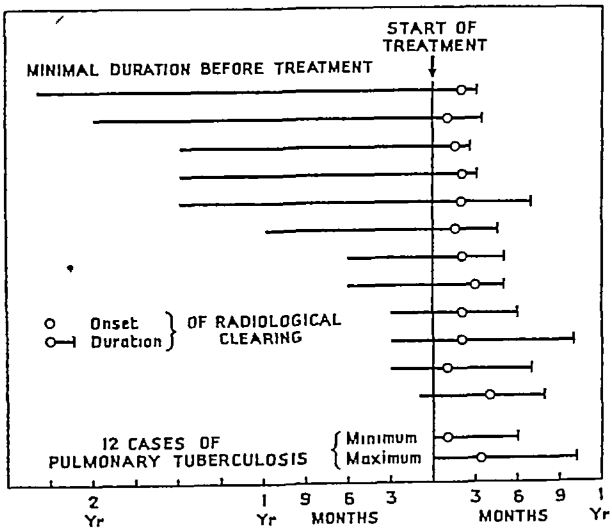

Fig 4—Results of streptomycin treatment of 12 cases of pulmonary sarcoidosis compared with those of 12 cases of pulmonary tuberculosis

Serial liver biopsies were taken from 8 patients in this series In 3 the sarcoid follicles completely disappeared during treatment In 3 others the follicles became less numerous, smaller, and more fibrous (fig 6) in the remaining 2 the follicles were fewer but larger and contained more hyaline material

19 of the 20 patients in this series were followed after treatment, up to three years in the earliest cases (table III) Of the 16 whose pulmonary lesions improved 11 relapsed completely and 4 partially, all within two months The remaining 1 is fit and has a normal radiograph six months after completing treatment Eventually 3 of those who relapsed had an even more abnormal radiograph than before cortisone was given 3 patients with advanced disease, who neither improved nor deteriorated during treatment, died six to eighteen months later, apparently in the natural course of their illness

It is evident that the use of cortisone and streptomycin for a short period usually confers only temporary benefit, especially on the lungs More prolonged treatment has therefore been tried 3 patients have now been treated for nine to eighteen months , all of them have, so far, maintained their initial improvement Fig 2 illustrates a typical example None of them has had serious side effects or shown evidence of progressive tuberculosis The eventual results of this prolonged treatment have yet to be assessed.

TABLE II—RADIOLOGICAL ASSESSMENT OF RESULTS OF TREATMENT OF PULMONARY SARCOIDOSIS WITH CORTISONE, STREPTOMYCIN, AND P.A S

| Duration of disease (yr ) | No treated | No change | Slight or moderate improvement | Great improvement |
|---|---|---|---|---|
| More than 2 | 11 | 3 | 7 | 1 |
| Less than 2 | 9 | 0 | 4 | 5 |
| Total | 20 | 3 | 11 | 6 |

## Discussion

There is no general agreement on whether any form of treatment is effective for pulmonary sarcoidosis It is difficult to judge the worth of any remedy, because of the variable duration and severity of the disease The problem is to avoid giving treatment unnecessarily to patients who may recover unaided, and yet not to delay it until permanent fibrosis prevents success In studying the effects of streptomycin and cortisone we have tried to allow for these difficulties by relating the effects of treatment to the duration of the disease

### *Streptomycin Treatment*

The first report of the use of streptomycin for pulmonary sarcoidosis was that of Pulaski and White (1948), who treated 7 patients for two to sixteen weeks without improvement Gendel et al (1952) have reported 6 cases treated for three to seventeen weeks without benefit, and Brun et al (1952) mention another On the other hand, Gernez Rieux et al (1948) reported a single success, and Hedvall (1950) reported 6 patients, all of whom improved during treatment for one to three months

The present results show that pulmonary sarcoidosis of more than about two years' duration is not affected by antibacterial therapy (table I) In 4 of our patients in this group, and in 2 others who were untreated, either

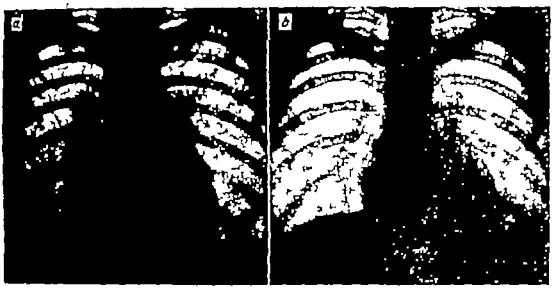

Fig. 3—Pulmonary sarcoidosis in a woman aged 26 : a before treatment and eighteen months after onset ; b after two months treatment with cortisone and streptomycin.

She had ten months history of iridocyclitis, loss of weight, and cough, and liver biopsy showed sarcoid follicles. After treatment there was complete radiological clearing and liver biopsy was normal

lung biopsy or necropsy confirmed the presence of severe pulmonary fibrosis (fig 7) On the other hand, more recent disease usually responded 9 of 15 such patients improved considerably The histology of the lung from 2 of our patients with recent disease shows that the infiltration is composed mainly of epithelioid cell follicles at this stage We have attempted to follow the histological changes by serial liver biopsies done in 9 patients who improved All of them had characteristic sarcoid follicles before treatment. The changes after treatment were variable and not consistent enough to be of much help in judging the progress of the individual case

The time of onset of radiographic improvement during treatment with streptomycin and P.A.S was closely related to the start of treatment (fig 4) This relationship counters the argument that improvement might have occurred naturally Also the time of onset of improvement and the period within which it was completed were similar in a group of patients with chronic pulmonary tuberculosis These similarities are compelling evidence that the common type of sarcoidosis in this country is a form of tuberculosis Others have found, as we have that streptomycin is by no means always effective The most obvious reason is that the disease is fibrotic and no recovery can then be expected However some of our early cases also did not improve A possible explanation is that the disease pattern of sarcoidosis has more than one origin Both these factors would have to be taken into account if a controlled trial with streptomycin were to be undertaken on a large scale

*Cortisone Treatment*

All accounts of the use of cortisone agree that it has a pronounced effect on most forms of sarcoidosis Reports so far have come mainly from the United States, where severe acute pulmonary sarcoidosis seems to be common (Siltzbach 1952 Lovelock and Stone 1953) These patients many of whom are Negroes have fever conspicuous breathlessness cough, and loss of weight as in 11 of the 14 cases reported by Shulman et al (1952) Our cases have been rather different severe constitutional symptoms were never seen and breathlessness only late in a chronic course In the absence of such features we have relied mainly on radiological changes for assessing the degree and permanence of any improvement

Our results from using cortisone with antibacterial therapy confirm the frequency, extent, and rapidity of radiographic improvement in the lungs in many cases However, there is some variation in the proportion improving as reported by other workers (table IV) Differences in dosage do not seem to be responsible Israel et al (1954) noted that patients with symptoms of less than six months duration improved much more than others Analysis of our cases according to the duration of the disease showed similarly that improvement was more frequent and complete when the disease was recent (table II)

Abnormalities of lung function estimated in the laboratory accord with the severity of any disability Patients with recent disease and negligible symptoms usually have normal lung function Those with older and more fibrotic disease show hyperventilation at rest and reduced

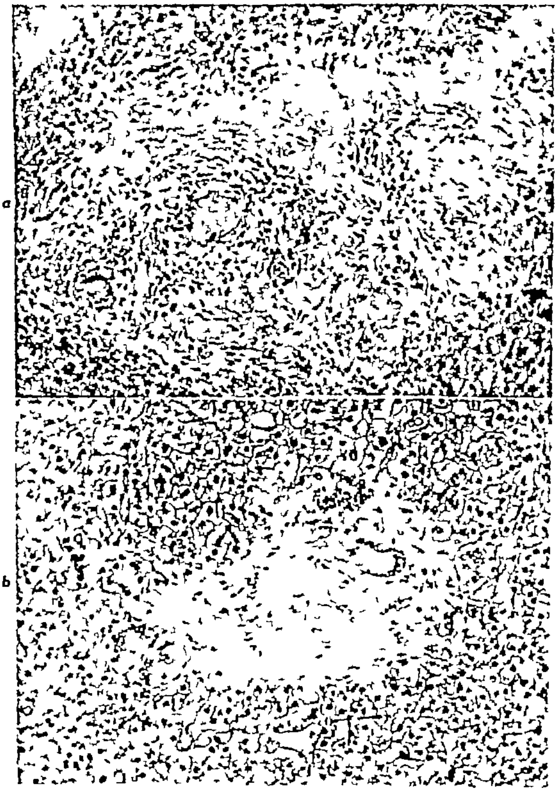

Fig 4—Biopsy specimen of liver from same woman as in fig 3 : a before treatment ; b after two months treatment with cortisone and streptomycin. There is absorption of cellular exudate and condensation of fibrous tissue present before treatment. (Hæmatoxylin and eosin × 140.)

TABLE III—RADIOLOGICAL ASSESSMENT OF RELAPSE AFTER TREATMENT OF PULMONARY SARCOIDOSIS WITH CORTISONE, STREPTOMYCIN, AND P.A S

| Duration of disease (yr ) | No treated | No improved | Relapse | | No remaining improved |
|---|---|---|---|---|---|
| | | | Partial | Complete | |
| More than 2 | 11 | 8 | 1 | 7 | 0 |
| Less than 2 | 8 | 8 | 3 | 4 | 1 |
| Total | 19 | 16 | 4 | 11 | 1 |

maximal breathing capacity The total lung volume and its subdivisions are diminished, and usually there is no evidence of emphysema Occasionally, when there is advanced disease, bronchial obstruction leads to over inflation of the lungs (Lukas 1951, McClement et al 1953) When this is due to bronchospasm, cortisone may give symptomatic relief, as happened in 1 of our patients These abnormalities of lung function are similar to those which other workers have found (Baldwin et al 1949, Galdston et al 1951) However, it requires the elaborate technique devised by Riley et al (1951) to detect the most important defect in lung function in this disease, which is a delayed diffusion of gas across the alveolar membrane (Riley et al 1952) Estimation of the oxygen gradient between alveolus and capillary is the most sensitive method of following the physiological changes during treatment It was not available for our investigations, which therefore only show that the ordinary tests in current use are not sensitive enough to detect changes during treatment in most instances Moreover even the more detailed method has not so far helped in selecting cases most likely to respond to cortisone—a decision which must be made chiefly from the duration and severity of symptoms and from the radiographic appearances

Some of our patients with pulmonary sarcoidosis have had serious lesions elsewhere Uveitis is often a grave manifestation of the disease and may in a short time seriously impair vision It has been found to respond well to cortisone Shulman et al (1952) reported 9 examples of active uveitis, all except 1 responding well to corticotrophic hormone or to cortisone, though 5 relapsed and required further treatment Ainslie and James (1953) have reported 4 other examples 2 with anterior uveitis were controlled with local cortisone, and 2 with more posterior lesions required systemic cortisone followed by local treatment to control the inflammation 4 of our patients who had uveitis responded well, the active inflammation subsiding in two weeks They have all had cortisone for at least four months 2, with serious lesions, for six and eighteen months, the other 2 are well two and six months after the end of treatment The risk of relapse seems to affect eye lesions just as frequently as other forms of sarcoidosis, and prolonged treatment, either local or systemic, is often required

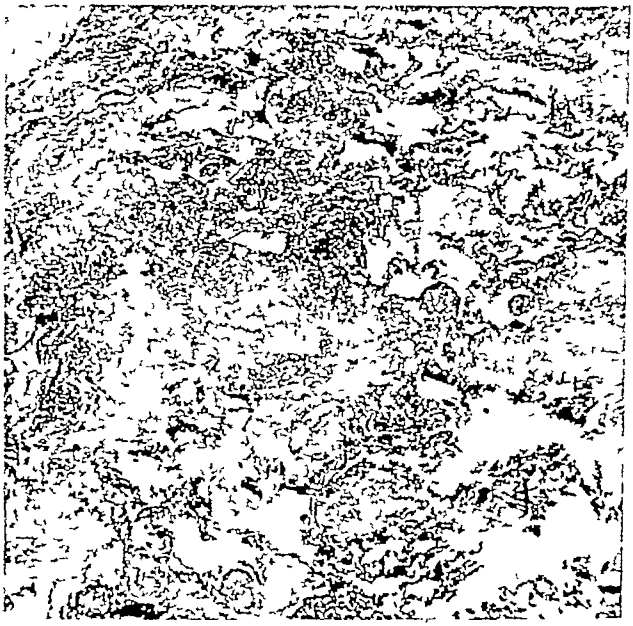

Fig 7—Biopsy specimen of lung showing extensive fibrosis with few persisting epithelioid cell follicles from a woman aged 53 who had pulmonary sarcoidosis for three years. (Hæmatoxylin and eosin × 25 )

Accounts of the effects of cortisone on the follicles of sarcoidosis are limited to a few biopsy reports, chiefly on lymph-nodes and skin Siltzbach (1952) did biopsies in 8 of his 13 cases before and after treatment with cortisone, but not on the liver In 5 the follicles were replaced by hyalinised fibrous tissue, 2 of these showed remains of granulomatous lesions 3 were unchanged Lovelock and Stone (1953) twice found similar substitution by hyaline connective tissue at the site of Kveim reactions A pronounced effect on the hepatic disease was seen in 8 of our patients given cortisone Sarcoid follicles in the liver either disappeared or became smaller and fibrotic during treatment From this it is reasonable to deduce that absorption of cellular sarcoid follicles is a chief cause of radiological clearing in the lung fields Residual shadows are due mainly to persistent fibrosis, as shown in our series by a lung biopsy after treatment (fig 7) and by necropsies Our observations of serial liver biopsies show an increase of fibrous tissue which is apparent rather than real, it is due to the disappearance of the cellular elements from the follicles, with condensation of existing fibrous tissue (fig 4*a* and *b*) The increased fibrosis which has been noted in recessive lymph nodes (Siltzbach 1952) is probably due to the same process We have not found any evidence that treatment with cortisone produces an absolute increase of fibrous tissue On the contrary, it is likely that cortisone, by suppressing the cellular follicles of sarcoidosis, prevents further fibrosis in the organs involved

TABLE IV—RADIOLOGICAL ASSESSMENT OF RESULTS OF TREATMENT OF PULMONARY SARCOIDOSIS WITH CORTISONE OR WITH CORTICOTROPHIN

| Reference | No treated | No improved radiologically | 3 mos after treatment | | | No remaining improved |
|---|---|---|---|---|---|---|
| | | | Relapse partial | Relapse complete | No record | |
| Michael (1951) | 5 | 5 | 0 | 5 | 0 | 0 |
| Small (1951) | 3 | 3 | 1 | 0 | 0 | 2 |
| Shulman et al (1952) | 10 | 8 | 2 | 3 | 1 | 2 |
| Siltzbach (1952) | 7 | 4 | 1 | 0 | 2 | 1 |
| Carstensen and Norvilt (1953) | 12 | 6 | 0 | 0 | 0 | 6 |
| Lovelock and Stone (1953) | 7 | 6 | 0 | 1 | 0 | 5 |
| Israel et al. (1954) | 26 | 17 | 3 | 6 | 0 | 8 |
| Present series | 19 | 16 | 4 | 11 | 0 | 1 |
| Total | 89 | 65 | 11 | 26 | 3 | 25 |

The risks during treatment of sarcoidosis with cortisone do not differ from those met with in other diseases, with one possible exception There is experimental evidence that cortisone reduces resistance to *M tuberculosis* (Hart and Rees 1950), and because of the possible association between this organism and sarcoidosis we felt it wise to give streptomycin as well Although more than 100 cases treated with cortisone alone have now been recorded, only 5 have developed tuberculosis Lovelock and Stone (1953) reported 4 of these where the diagnosis of sarcoidosis is doubtful, and Small (1951) another The evidence suggests that the risk has been exaggerated.

It is difficult to discover from most reports how often the pulmonary disease has relapsed when treatment has ceased. Michael (1951) stated unequivocally that 5 out of 5 patients reverted radiographically and symptomatically to their former state Shulman et al (1952) reported 10 patients with pulmonary sarcoidosis 8 of whom improved 5 relapsed to some extent Some of these were treated again on two or three occasions, but they were not followed long enough for us to be sure of the final outcome Lovelock and Stone (1953) report the best results, with 5 out of 6 remaining improved after several months observation Israel et al (1954) report that only 8 of their 26 patients with pulmonary sarcoidosis have not relapsed Our figures are even more disappointing 11 of 16 patients relapsing completely within three months (tables III and IV) The rate of relapse is so high that short-term treatment offers little hope of controlling sarcoidosis However as our results so far have shown, more prolonged treatment is practicable and can maintain improvement Should relapse still occur continuous treatment will be needed by some patients.

There was a higher proportion of relapses after antibacterial treatment with cortisone than after antibacterial treatment alone Of 12 patients who responded to streptomycin and P.A.S 9 have had lasting radiographic improvement, whereas of 16 patients who responded to cortisone only 5 did the same We cannot explain this unexpected difference though there are several possible explanations One is that the improvement of some of the patients during treatment with streptomycin and P.A.S alone was fortuitous we have already given reasons for believing this to be improbable Another possible explanation is that cortisone may have had an adverse effect on the resistance of the host to the unknown cause of sarcoidosis or on the susceptibility of the causal organism to antituberculous drugs although its suppressive effect on the epithelioid cell follicle was dramatic

Our experience is that the treatment of pulmonary sarcoidosis is still unsatisfactory partly because of the difficulty of deciding when it should be given and partly because of its restricted value We consider that patients whose sarcoidosis is recent and symptoms are minor can usually be observed with safety because many will improve spontaneously within a year If however there is no radiographic improvement by then, there is less prospect of natural remission so our practice now is to begin treatment about this time We use streptomycin with P.A.S or isoniazid for three months continuing subsequently as long as there is radiographic response If there is no improvement in three months we consider whether to give cortisone as well The long period during which it may be necessary to give it and the consequent inconvenience demand that cortisone should be used only when there is a real need to control progressive changes in the lungs, eyes or elsewhere A dosage of 100–150 mg daily is usually sufficient. After one to two months this dosage is steadily reduced until the minimal effective dosage is found This treatment is then continued for at least a year Cortisone is also used initially for patients whose disease when first seen is already severe and therefore more likely to have a bad prognosis When the sarcoidosis is extensive and of long standing with much fibrosis neither form of treatment is likely to be of use

## Summary

Pulmonary sarcoidosis was treated with streptomycin and P.A.S (30 cases) and with cortisone in addition (20 cases)

Patients whose disease had been present for more than two years seldom improved (1 in 9) during treatment with streptomycin and P.A.S whereas those with a shorter history often improved (11 in 21) The time of onset of radiographic improvement and of its greatest extent was similar to that of chronic pulmonary tuberculosis treated in the same way 3 of the 12 who responded to treatment relapsed subsequently

When cortisone was given as well 17 of 20 patients improved radiographically Regression of sarcoid follicles in the liver was seen in 8 patients who had serial biopsies Improvement took place more rapidly than that from streptomycin and was also more frequent and more complete among those with recent disease After treatment 11 patients relapsed completely and 4 partially Prolonged treatment up to a year was found to be safe and effective

We are much indebted to colleagues who referred patients to our care and to Prof H. A Magnus and Dr J Clegg for their advice and for technical help with the morbid histology We wish to thank the Medical Research Council for some of the supplies of cortisone Dr F J Prime for making and interpreting investigations of lung function and Dr L G Blair for independent assessment of the radiographs. Some of our expenses were defrayed by a grant from the research fund of King's College Hospital and one of us (J D) was in receipt of a personal grant from the research fund of Brompton Hospital

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# SPASTIC PARAPLEGIA OF MIDDLE AGE*

## A CLINICOPATHOLOGICAL STUDY

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MIDDLE AGED patients with spastic paraplegia which has come on gradually and has progressed slowly are commonly seen in neurological clinics and may present a difficult diagnostic problem A carefully recorded history and complete examination combined with ancillary investigations, often give a clue to the underlying lesion Thus there may have been an episode of diplopia in the past; or the illness diagnosed as a chill on the kidneys may on closer questioning be revealed as a neurogenic disturbance of the bladder But not infrequently the pathological diagnosis remains obscure

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* Honyman Gillespie lecture given at the University of Edinburgh Nov 18 1954

Some idea of this difficulty is given by the different diagnostic fashions which have prevailed from time to time. Thus, in the 1870s and 1880s primary lateral sclerosis was the favourite diagnosis, but in 1892 Erb described syphilitic paraplegia which then took pride of place. Then at the turn of the century Russell et al (1900) described subacute combined degeneration of the cord, which became the popular diagnosis, but in turn was replaced about 1910 by disseminated sclerosis. Later, with the rise of neurosurgery, every case of spastic paraplegia became a tumour suspect. The present time is not without its fashion also, for some observers now regard all these patients as suffering from cervical spondylosis, which can be demonstrated all too readily in radiographs of the cervical spine in this age group.

These difficulties have led to the recognition of a group of cases termed "spastic paraplegia of uncertain ætiology," which is discussed here. Little is known about the natural history of this condition. What becomes of these patients? How long do they live? How many die with the disorder still undiagnosed, and how many with the passage of years develop symptoms or signs which enable a pathological diagnosis to be made?

In the early stages of the disease these patients are usually seen in a neurological clinic, and for a time they may be followed up. But with the passage of months or years they are either lost from the follow-up or, as walking becomes more difficult for them, they cease to attend. They then find their way to the chronic wards of general hospitals or to homes for incurables, or else they remain at home under the care of their general practitioner, being nursed by the district nurse or by relatives. So those who see them in the early stages of the illness never know the outcome, and those who care for them in the latter part of the illness have often little interest in its onset and development. It is hardly surprising that post-mortem examinations are few and far between.

## Criteria and Material

In dealing with a condition so vaguely defined as this, it was necessary to adopt criteria to determine which cases should come under the heading of spastic paraplegia of uncertain ætiology. Arbitrarily, it was decided that the paraplegia must appear after the age of 20, and be of gradual onset and slow progression. Thus acute paraplegia from any cause and congenital paraplegia were excluded. Bilateral extensor plantar responses were a sine qua non for the diagnosis. Further signs of pyramidal defect, and also sensory loss and sphincter disturbance, might or might not be present. Pyramidal signs in the arms did not exclude the case from the series, but cases were excluded in which there was evidence of a lower motor neurone lesion in the upper or lower limbs, sensory loss in the arms indicative of a root lesion, or any indication that the cranial nerves were involved.

An attempt was made to overcome the difficulties of follow-up by culling the material from two sources.

1. The first source consisted of the records of all the patients who had been under the care of Dr Arnold Carmichael at the National Hospital, Queen Square, between 1930 and June, 1952. From this source 80 cases were found that fulfilled the criteria.

2. The second source was the records of post-mortem examinations at the National Hospital, Queen Square, from the years 1928 to June 1952. These records were searched, and a list made of all the patients who had died from any disease that might have conceivably presented at some time as spastic paraplegia. The clinical records of these patients were then studied, and if in fact they had presented as spastic paraplegia of uncertain ætiology at one stage in their clinical history they were included in the study. 35 cases were obtained from this source.

By this method, therefore, 80 cases whose natural history might be followed, and 35 cases in which the patient had died but whose clinical history was available, were obtained.

## Findings

This study had three aims. The first was to discover the natural history of spastic paraplegia appearing for the first time in adult life. The second was to ascertain, as far as possible, the underlying pathological processes. The third was to endeavour to establish criteria which might facilitate prompt recognition of the cause of the paraplegia.

### CLINICAL SERIES

The 80 cases from Dr Carmichael's records (the "clinical" series) were followed up as follows:

| | |
|---|---|
| Seen personally | 46 |
| Information obtained by post | 6 |
| Dead | 9 |
| Untraced | 19 |

9 patients had died, but post-mortem examination had been done in only 1 case.

This examination was made on the instructions of a coroner. The pathologist confined his attention to the thoracic and abdominal viscera, establishing a diagnosis of coronary occlusion, but the brain and spinal cord were not removed.

The average age of the 52 traced survivors when their symptoms first appeared had been 40 years, though there was rather a wide scatter from 20 to 70 years. At the time of the follow-up the average duration of the illness was 10.4 years, the shortest duration was 1 year and the longest 40 years. In a majority the duration was over 5 years, which clearly confirms that this is indeed a chronic condition.

TABLE I—DIAGNOSIS IN 52 CASES STILL ALIVE

| Diagnosis | No. of cases |
|---|---|
| Disseminated sclerosis | 10 |
| Tumour | 7 |
| Prolapsed disc | 3 |
| Syringomyelia | 1 |
| Cervical-cord lesion | 2 |
| Paraplegia with dementia | 4 |
| Unknown ætiology | 25 |

When these 52 patients were re-examined it became clear that they could be divided into two groups: (1) 27 in whom, with the passage of time, the diagnosis had become apparent, and (2) 25 in whom the diagnosis was still obscure (table I).

*Manifest Causes*

The following is a case, in the first of these two groups, in which disseminated sclerosis became manifest.

A young woman, aged 24, began to have hesitancy of micturition, followed a year later by weakness of the legs with stiffness, which slowly progressed. She had no remissions, and her symptoms became steadily worse. Eight years after the onset she was admitted to the National Hospital, under the care of Dr Carmichael, but, despite most careful observation, the cause of the spastic paraplegia could not be detected. Investigations included radiography of the spine, examination of the cerebrospinal fluid, and myelography, all of which revealed no abnormality. She was re-examined some three years later, by which time she was very euphoric and had developed severe dysarthria. There was bilateral intention tremor in the hands, and, in addition to the spastic paraplegia, she had lost vibration and position sense in both feet and was grossly ataxic. Thus in the tenth and eleventh years of her illness this patient quickly developed widespread signs which, for the first time, clearly indicated disseminate lesions.

In the following case signs of syringomyelia appeared.

The patient, when aged 55, began to have stiffness and weakness of the legs, and on examination two years later he had a moderately severe spastic paraplegia with only slight impairment of vibration sense and no other sensory loss. Thirteen years later, he was bedridden because of the paraplegia, and had also typical dissociated sensory loss from

TABLE II—POST MORTEM DIAGNOSIS IN 35 CASES

| Diagnosis | No of cases |
|---|---|
| Disseminated sclerosis | 12 |
| Tumour | 11 |
| Prolapsed disc | [illegible] |
| Syringomyelia | 3 |
| Paget's disease | 1 |
| Subacute osteitis | 1 |
| Spinal deformity (non tuberculous) | 2 |
| Hypertrophic pachymeningitis | 1 |
| Aneurysm of intervertebral artery | 1 |
| Defect in anterior spinal artery | 1 |

the trigeminal area to the second thoracic dermatome on the left, and from the second cervical to the first thoracic dermatome on the right

In 4 patients dementia developed after paraplegia raplegia developing consecutively with dementia has en well known since Lhermitte s (1907) description of *paraplegie des vieillards* Moreover dementia followed paraplegia is a not uncommon sequence The present oup is unusual in that the paraplegia preceded the mentia by a very long time the shortest interval as 7 years and the longest 16 years The clinical ture in these cases was also remarkably uniform

The paraplegia appeared in the 5th decade and the dementia the 6th. The paraplegia was predominantly motor sensory s being confined to slight impairment of vibration sense d the dementia had the same features in all 4 patients, fecting mainly the intellectual aspects of mental life and aring the affective In the 3 patients submitted to pneumo cephalography symmetrical dilatation of the lateral ntricles with enlarged cortical sulci was found

Possibly these were simply cases of spastic paraplegia which dementia happened to develop but the incidence 4 cases in a series of 52—that is about 8%—suggests at this condition may be a nosological entity If so e paraplegia was possibly due to a degenerative lesion the paracentral lobules of the cerebral hemispheres nd in time the degenerative process spread beyond the bules to involve the whole of the cerebral hemispheres, ving the eventual picture of paraplegia and dementia at since none of these cases have been examined post ortem the nosology is still uncertain

*ause Unknown*

In the 25 cases where the diagnosis remained obscure he average duration of the disease was 13 years com ared with 10 years for the whole clinical series In this oup the disease had progressed slowly and relentlessly ntil, at the time of follow up over a quarter of them ere either bedridden or reduced to a wheel-chair life The remainder got around with difficulty on sticks

The most protracted case illustrates strikingly how ronic the condition could be without a diagnosis ever eing reached

This man first noticed dragging of his left leg in 1912 when was 31 years of age followed 9 months later by a similar agging of his right leg The symptoms progressed slowly er the years, and in 1930 at one of many examinations had severe motor paraplegia with no vestige of sensory loss rmal radiographs of the spine and normal cerebrospinal id. He was examined in the course of this study 22 years ter when he was 71 years old. He had complete motor raplegia, but could feel the lightest nylon thread or faintest pprick on his toes, though he had lost vibration sense in the et. His mental faculties were unimpaired and his sphincters mpletely unaffected, and he looked as though he would ntinue thus for another thirty years

The majority of these 25 patients were thoroughly investigated in the course of this study including full ood examinations fractional gastric analyses lumbar nctures and radiographs of the spine and myelo aphy was done in 10 cases In no case was further light rown on the underlying lesion It is a chastening ought that despite our best diagnostic endeavours, lf of the group of 52 patients still defied diagnosis ten more years after the onset of the illness.

NECROPSY SERIES

The findings were much the same in the 35 cases collected from necropsy records (table II) The average age at the onset of the illness was 43 compared with 40 years in the clinical series and the average duration of the illness at the time of death was 7 years, compared with the 10 years duration to follow up in the clinical series In all respects the groups were comparable, the illness appearing in the same manner and progressing in the same way

Not all of these cases had remained undiagnosed until after death In about two thirds a pathological diagnosis had been reached before death but in the remaining third the diagnosis was spastic paraplegia of unknown ætiology until the pathologist revealed the cause of the paraplegia which he did in every case Nor was it only rare lesions such as aneurysm of the intervertebral artery that had remained undiagnosed for half of the cases of disseminated sclerosis were not diagnosed ante mortem. This was not surprising since clinically there was nothing to indicate disseminate lesions and in 4 of the cases there was no trace of sensory impairment in the feet

The findings in the necropsy series, therefore, accord with those in the clinical series In round figures a third of the patients had disseminated sclerosis and a third compression of the spinal cord from tumours or prolapsed intervertebral discs the remaining third had a hetero geneous group of conditions some rare Neither subacute *combined degeneration of the cord nor motor* neurone disease was found in either the post mortem or the clinical series probably because these conditions are more easily diagnosed even in the early stages

## Diagnosis

These two series confirm the difficulty of distinguishing disseminated sclerosis from spinal tumour In only 1 of the 12 cases of disseminated sclerosis in the necropsy series was pain a symptom—and this was only a vague ache in the lumbar region—but pain occurred in *only* 7 of the 11 patients with tumours All the patients with a tumour had a clear-cut sensory level but 8 out of 18 patients without tumours who had sensory loss also had a sensory level Nor did the complete absence of sensory loss exclude disseminated sclerosis in the post mortem group disseminated sclerosis was found in no less than 4 out of 6 cases where there had been no sensory loss The most helpful points in the differentiation of disseminated sclerosis from spinal tumour in the early stages were (1) the level of the protein in the cerebrospinal fluid which was above 100 mg per 100 ml. in all but 1 of the cases of tumour whereas in disseminated sclerosis it was never above 60 mg per 100 ml and (2) the result of myelography which was abnormal in all the 18 patients with spinal tumour

It seems quite clear that conditions such as dissemi nated sclerosis syringomyelia and spinal tumour can present as spastic paraplegia in the first instance and even the most exhaustive investigations will reveal nothing further The primary disease will sometimes declare itself sooner or later—sooner in the case of tumour later in the case of a non-compressive lesion—but in between a third and a half the causal lesion will not be established ante mortem

These series suggest that cervical spondylosis is an unusual cause of spastic paraplegia Of the 87 cases in the combined clinical and post mortem groups only 5 were found to be due to cervical spondylosis and of the 35 cases in the post mortem group where the evidence is more incontrovertible only 2 (about 6%) were due to this cause The post mortem series collected mainly during a period when there awareness of cervical spondylosis but the fac examples were found at necropsy indicates that the condition was not unsought, and if spondylosis was being overlooked some cases would have remained undiagnosed, whereas a pathological diagnosis was established in every case. The incidence of radiographic evidence of cervical spondylosis in middle aged patients who have no neurological signs is unknown, but it is apparently fairly high. When such evidence is associated with spasticity of the legs, it should not be supposed that the one disorder is necessarily the cause of the other.

### Summary

52 cases of “spastic paraplegia of unknown ætiology,” first examined between 1930 and 1952, were followed up. A further 35 cases were collected from necropsy records. The findings in these two series accord with each other.

Some ten years after onset the cause of the disorder had declared itself in about half the cases; the commonest causes were disseminated sclerosis and tumour. In about a third of the cases the cause was not recognised ante mortem.

Cervical spondylosis was a rare cause of this syndrome.

I thank Dr. E. A. Carmichael for encouragement with this study and for access to his records, and Dr. J. G. Greenfield and Dr. W. Blackwood for allowing me to use their post-mortem records.

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## TETRACYCLINE IN TYPHOID FEVER

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CHLORAMPHENICOL is generally accepted as the most effective of the antibiotics used in the treatment of typhoid fever. But though usually the response is excellent, occasionally it is very disappointing: of 120 patients with typhoid whom we treated with chloramphenicol, 7% showed no apparent response or only a very slow one (Watson 1953).

We have often been able to isolate *Salmonella typhi* from blood clots of patients undergoing treatment with chloramphenicol: in one case the organism was isolated after 22 g. had been given, and in another after 10 g. (Watson 1955). Goodpasture (1937) and Adams (1939) have shown that *S. typhi* are present in plasma cells in intestinal and mesenteric lesions, and we believe that these intracellular forms are responsible for the transient episodes of bacteræmia. The observations of Smith et al. (1949) on the effect of chloramphenicol on the esterase of animal mitochondria suggest that the cell wall forms a barrier which prevents the antibiotic from acting on intracellular forms.

Chloramphenicol also gives rise to a number of toxic effects, including nausea, vomiting, stomatitis, glossitis, skin rashes, and mental apathy (El Ramli 1950). In a series of 330 cases of typhoid fever reported by Marmion (1952), the incidence of toxic reactions was as high as 44%. Lately, agranulocytosis has been reported with disturbing frequency.

In view of these observations we have treated a number of cases of typhoid fever with tetracycline.

Tetracycline is chemically related to chlortetracycline (aureomycin) and to oxytetracycline (terramycin), and is usually prepared by catalytic hydrogenation of chlortetracycline (Boothe et al. 1953). Its spectrum of activity is similar to that of the two derivatives, and cross resistance between the three antibiotics has been reported (Finland et al. 1954).

Tetracycline appears to have two advantages over the chlor- and oxy- derivatives—namely, greater penetration of body tissues (Wright et al. 1953) and a lowered incidence of toxic effects (Putnam et al. 1953). Of 118 patients treated by Finland et al. (1954) with tetracycline, 110 were free from toxic effects, 1 case developed stomatitis, and 7 had mild diarrhœa.

### Case-records

The cases reported here were sporadic ones arising in an area where typhoid fever is endemic. All showed the typical clinical features of the illness.

**Case 1.**—A Bantu, aged 7, was admitted on the 11th day of illness. He was grossly dehydrated, with a temperature of 103°F and pulse-rate of 124 per min. *S. typhi* was isolated from blood clot and from whole blood. Cultures of stool and urine were repeatedly negative.

Tetracycline 250 mg. 6-hourly by mouth was begun on the day of admission. The response was poor: he continued for 12 days to run a temperature of 101–103°F and there was scarcely any clinical improvement. Between the 12th and 20th days of treatment there was a slow improvement in his clinical state, but he continued to run a temperature of 99–100°F. During the 4th week improvement became more rapid, and his temperature remained normal. Tetracycline was continued for 12 days after he became afebrile.

**Case 2.**—A Bantu, aged 14, was admitted with 2 weeks' history of illness; his temperature was 102°F and his pulse-rate 140. *S. typhi* was cultured from both whole blood and blood clot. Cultures of stool and urine were repeatedly negative.

Tetracycline 250 mg. 6-hourly was given from the day of admission. The temperature remained elevated for 9 days, with no clinical improvement for the 1st week, during which he was dull and apathetic. Between the 9th and 12th days the headache and anorexia which were present on admission gradually disappeared, but abdominal distension persisted for about 8 more days. He became afebrile on the 9th day and tetracycline was continued for 14 days from the day of becoming afebrile. Subsequent progress was satisfactory.

**Case 3.**—A Bantu female, aged 17, was admitted after 14 days' illness. She was confused and irrational. Her temperature was 101°F and her pulse-rate 100. *S. typhi* was isolated from blood clot after 24 hours' incubation, but culture of whole blood in bile broth was sterile after 3 weeks' incubation. The cerebrospinal fluid (C.S.F.) showed no abnormality.

Tetracycline 250 mg. 6-hourly was given from the day of admission. No improvement was noted during the first 10 days. She continued to run a temperature of 99–101°F and remained disorientated, with occasional outbursts of maniacal behaviour. In view of these outbursts the C.S.F. was twice examined again, but was normal. On the 11th day of treatment she became afebrile, and her mental state improved greatly during the next 2 days. Abdominal distension persisted for a further 3–4 days. Improvement was maintained, tetracycline being given for 12 days from the day of becoming afebrile.

**Case 4.**—A Bantu, aged 12, was admitted on the 4th day of his illness. His main complaint was of severe frontal headache. He had a temperature of 104·8°F and a pulse-rate of 110. *S. typhi* was isolated from blood clot after 24 hours' incubation, but whole blood culture was sterile after 3 weeks' incubation.

Tetracycline 500 mg. 6-hourly was started on the day after admission, but for the next 5 days his condition deteriorated, with a temperature of 102°–104°F. On the 6th day it seemed unjustifiable to continue tetracycline further. Chloramphenicol was therefore given instead, 500 mg. 6-hourly. During the next 3 days there was a notable improvement, the temperature falling to normal on the 5th day of chloramphenicol treatment. Subsequent improvement was maintained, chloramphenicol was continued in the same dosage for 10 days from the day of becoming afebrile.

**Case 5.**—A Bantu, aged 16, was admitted in a delirious state, with a temperature of 103°F and pulse-rate of 100, probably about the 8th day of illness. *S. typhi* was isolated from blood clot and from whole blood culture. Cultures of stool and urine were repeatedly negative.

Tetracycline 500 mg. 6-hourly was given from the day of admission. The temperature remained elevated for a further 5 days, and during the first 4 there was no change in the clinical state. During the following week there was a slow improvement. Though this patient appeared to respond rather better than those already considered, there was no dramatic improvement such as is seen with chloramphenicol.

Case 6.—A Bantu aged 8 was admitted extremely ill with a temperature of 103 2°F and pulse-rate of 100 He had been ill for 7 days. *S typhi* was isolated from blood-clot after 24 hours incubation, but routine whole-blood culture was sterile after 3 weeks. Stool and urine cultures were repeatedly negative

This boy was first treated for 14 days with chloramphenicol 250 mg 6-hourly As there was no improvement tetracycline 500 mg 6 hourly was substituted. A very slow clinical improvement followed but the temperature remained elevated till the 7th day of tetracycline therapy and abdominal distension persisted for a further 3 days. Tetracycline was continued for 17 days in all

### Discussion

The cases in this series were unselected consecutive admissions to the medical wards of a general hospital None responded to tetracycline in the way that such cases usually respond to chloramphenicol Pyrexia persisted on the average, for 8–9 days after the start of treatment (In a series of 120 cases which we treated with chloramphenicol the corresponding figure was 4 1 days. El Ramli (1950) recorded 3 5 days in a series of 200 cases treated with chloramphenicol ) Clinical improvement was correspondingly poor

These findings are not wholly unexpected since the response of typhoid fever to chlortetracycline has also been disappointing Werner et al. (1954) demonstrated that in vitro strains of *S typhi* show somewhat similar sensitivity to chloramphenicol and to chlortetracycline but that, in vivo chlortetracycline is less effective They attribute this to some difference in the drug host relationship I have examined the in vitro sensitivity of 20 freshly isolated strains of *S typhi* to chloramphenicol and to tetracycline and have found almost identical minimum inhibitory concentrations

Case 6 showed no response at all to chloramphenicol and is similar in this respect to cases described previously (Watson 1953) The slow improvement that followed tetracycline therapy took place during the 5th week of the illness and was probably due to a host response more than to specific antibiotic therapy

In addition to these 6 patients we have treated a chronic fecal carrier of *S typhi* with tetracycline 250 mg 6-hourly for 10 days. During this period daily stool-cultures were negative and they remained so for 7 days thereafter Subsequently however they became positive again

In none of the patients were any toxic effects observed, and all tolerated the drug well. But small though the series is, the results suggest that tetracycline is not a suitable substitute for chloramphenicol in the treatment of typhoid fever

### Summary

Six patients with typhoid fever were treated with tetracycline The response observed was poor and for the treatment of this disease tetracycline seems to be considerably less useful than chloramphenicol.

I wish to thank Dr J Parker medical superintendent of Edendale Hospital, for permission to publish these case-notes The tetracycline was supplied by Messrs. Lederle

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# PATTERN OF THE HUMAN TONGUE

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ALTHOUGH the tongue lends itself readily to observation as is evident from the antiquity of the custom of inspection of the tongue in clinical medicine, little work seems to have been published on the finer details of the tongue's surface as seen in health and disease Indeed it was not until modern investigation of nutrition showed that the lingual mucosa undergoes well marked changes in nutritional deficiency that attention was drawn to the mucosal pattern and to the devising of methods for recording it

This paper deals with the tongue pattern found by investigation of 1098 apparently healthy persons of European Tswana Hottentot Swazi or Bushman origin Of these, 822 were Tswana (indigenous inhabitants of the Bechuanaland Protectorate) 90 Europeans residing in the Protectorate 82 Hottentots from Kaartlwe, Bechuanaland Protectorate (one of the very few remaining Hottentot settlements), 79 Swazis from the Mbabane district of Swaziland and 25 Bushmen from the Southern Kalahari.

The tongue pattern is due to three anatomical components on the anterior two thirds of the lingual dorsum (which region alone can be recorded by the method used): the filiform papillæ the fungiform papillæ, and the mucosal fissures The papillæ are projections of the corium The filiform papillæ are thickly distributed over the dorsum the fungiform papillæ larger than the filiform, are found at the sides and apices of all tongues and in many tongues they are also spread more or less thickly over the anterior two thirds of the dorsum The fissures of the mucosa vary greatly in number, most tongues showing none whereas in a small proportion the entire surface may be covered with fissures of different sizes

### Method

Photography seems to have been the first method used for recording the features of the tongue's surface but it is expensive needs skill and does not provide easily decipherable records of the anatomical features of the tongue mentioned above

Other published methods involve the use of smoked paper (Oatway and Middleton 1932) Such records unless treated with a preservative—e g shellac—are not permanent

Di Palma (1946) described a method by which prints of the tongue's surface are taken with a special ink The method has been modified and a full account of the technique published elsewhere (Squires 1953) It need only be said here that the ink the essential ingredient of which is Evans blue, is applied to the extruded tongue with a squeegee or a piece of gauze and impressions are taken by pressing a piece of glazed paper on the tongue Once the impressions are dry—i e after a minute or two—they are permanent Correctly produced prints emphasise the components of the tongue pattern in detail such as cannot be obtained by photography

### Discussion

In healthy people the filiform papillæ appear on the print as round or star-shaped dots the fungiform papillæ, which being smooth pick up little ink and that only on the sides and lateral crevices show up as round cheese holes The fissures pick up no ink, and are seen in outline only

On examination of large numbers of prints it becomes obvious that certain characteristics of the patterns are sufficiently constant to permit type grouping Di P

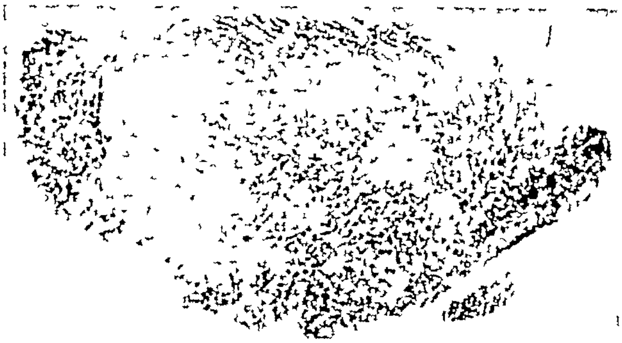


Fig 1—Filiform type

(1946) gave a list of five types of tongue pattern with one dominant feature and five further types with a secondary feature He provided, however, no criteria for distinguishing each of these groups It has been found possible to classify the present series into four groups, each exhibiting only one dominant feature which is easily recognised The classification is reasonably clear-cut, and there is little overlapping or ambiguity

The groups are classified as follows

(1) *Filiform* (fig 1), in which the filiform papillæ are uniformly and densely distributed all over the dorsum save at the apex and sides, which are occupied by fungiform papillæ

(2) *Fungiform* (fig 2), in which the fungiform papillæ, besides being present at the apex and sides, appear plentifully over the dorsum The criterion of a fungiform tongue is that the papillæ must be uniformly and thickly scattered over the dorsum, because most tongues of any group will show a few isolated fungiform papillæ among the filiform

TABLE I—DISTRIBUTION OF TYPE GROUPS IN WHOLE SERIES (1098)

| Filiform | Fungiform | Linear | Fissured |
|---|---|---|---|
| 831 (*76* %) | 205 (*19* %) | 43 (*4* %) | 19 (2 %) |

(3) *Linear* (fig 3), in which a linear arrangement of the filiform papillæ predominates

(4) *Fissured* (fig 4), in which well marked fissures occur The so called "scrotal" tongues are included in this group It is to be noted that one central fissure extending down the midline, which may occur naturally or else be caused by contraction of the tongue during the process of taking off a print, is not sufficient to include the tongue in this class

Table I indicates the frequency of occurrence of the various groups in the complete series of 1098 persons

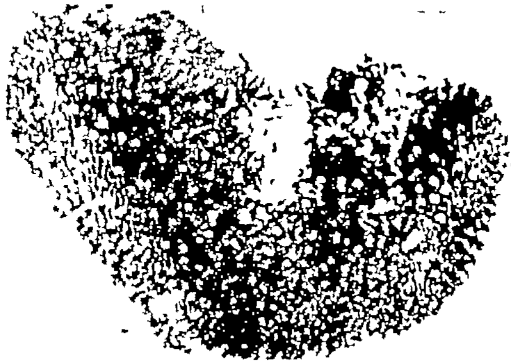


Fig 2—Fungiform type

It will be noted that group (1), the filiform, predominates and includes three quarters of the series

The patterns appear to be constant for any given healthy person According to Di Palma (1946) no two tongues give the same pattern, this finding has been confirmed for the present series, which included the patterns of a pair of identical twins These were dissimilar, although of the same type

Certain systemic diseases (e g, cardiac and nephritic œdema) can obliterate the pattern by causing swelling of the tongue, and chronic cachexial conditions (e g, pulmonary tuberculosis) can cause denudation of the tongue and consequent disappearance of the pattern, probably by upsetting epithelial metabolism

The effect of nutritional deficiencies on the pattern has been dealt with in detail elsewhere (Squires 1953) It will suffice to remark here that during the course of such disorders the filiform papillæ tend to disappear, and at a more advanced stage the mucosa becomes disorganised, giving rise to the well-known smooth tongue Provided that the deficiency has not lasted too long, the tongue changes are reversible, and tongue prints can be used for following the regeneration of the mucosa Fig 5 shows the pattern of an African adolescent after a few months' moderately severe food shortage, and fig 6 the pattern of the same tongue about seven months later, after a good crop season

Finally, there are some indications of racial variation in the incidence of the types, as shown in table II, in which the Bushman sample, although very small, is included for the sake of completeness and comparison If the Bantu (Tswana and Swazi), Hottentot, and European groups are compared, it will be seen that the difference between the incidence of fungiform tongues is impressive, indeed, between the Bantu and European

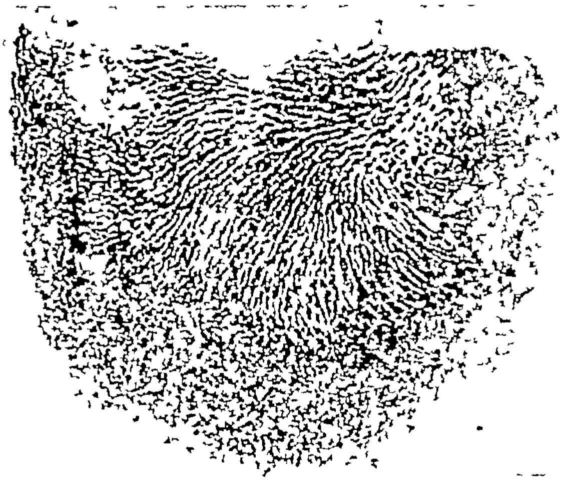


Fig 3—Linear type

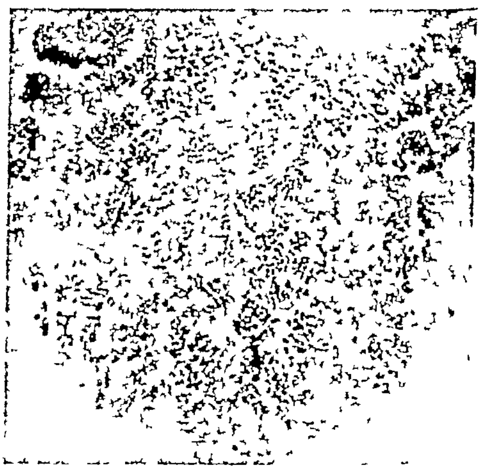


Fig 4—Fissured type.

TABLE II—RACIAL VARIATIONS IN DISTRIBUTION OF TYPE GROUPS

| Race | No | Filiform | Fungiform | Linear | Fissured |
|---|---|---|---|---|---|
| Tswana | 822 | 641 (78%) | 137 (17%) | 34 (4%) | 10 (1%) |
| Swazi | 70 | 53 (76%) | 11 (16%) | 3 (4%) | 3 (4%) |
| Hottentot | 82 | 60 (73%) | 19 (23%) | 2 (2%) | 1 (1%) |
| European | 90 | 57 (63%) | 28 (31%) | — | 5 (6%) |
| Bushman | 25 | 11 (44%) | 10 (40%) | 4 (16%) | — |

groups the difference is significant (In spite of the tenfold difference in numbers between the Tswana and Swazi groups, the proportion in which the types occur is practically identical ) The proportion of filiform to fungiform tongues among the Bushmen is also interesting but the series is far too small to justify speculation about its possible significance

## Summary

An account is given of the mucosal patterns of the healthy human tongue in 1008 persons as recorded by an ink printing method.

The persons examined were of Tswana, European Hottentot, Swazi, or Bushman origin

The tongue patterns can be divided into four types filiform, fungiform linear and fissured

The filiform type accounted for over 75% in the whole series, the fungiform for 19% the linear for 4%, and the fissured for 2%

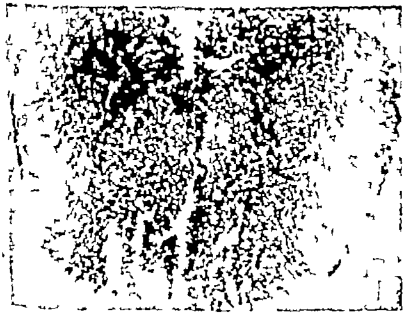
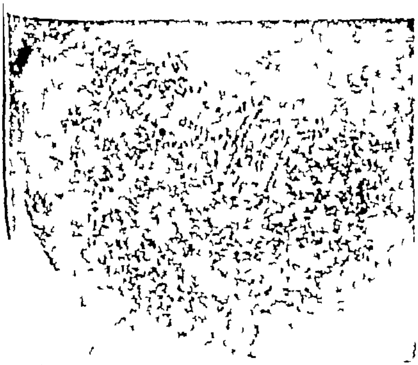


Fig. 5—Tongue pattern in chronic nutritional deficiency



—Same tongue as in fig 5 showing restoration of original pattern when nutritional deficiency has been made good.

No two tongues gave the same pattern a pair of identical twins gave dissimilar prints although they were of the same type

There is some evidence of racial variation in the incidence of type grouping

I am indebted to the acting director of medical services Bechuanaland Protectorate for permission to publish

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# HEPATIC ABSCESS SECONDARY TO DUODENAL ULCER

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Liver abscess caused by a penetrating duodenal ulcer is rare Heathfield (1942) described one case (diagnosed post mortem) where the abscess followed definite perforation of an ulcer A similar case recorded by Beaver et al (1946) was complicated by pleural effusion suppurative peritonitis, and thrombosis of the femoral vein The following case in which the abscess was produced by a peptic ulcer complicated by hæmatemesis and melæna, seems to have no reported parallel.

## Case-report

A Parsee aged 58 admitted to hospital on Jan 28 1954 for the past eight days had had pyrexia anorexia, and a feeling of heaviness in the abdomen His temperature had been observed to rise to 102 F each evening returning to normal in the morning

*Previous History*—Two years previously the patient had had a similar bout of intermittent fever the liver was then enlarged He had been given injections of penicillin for fifteen days followed by chloramphenicol and quinine for fifteen days The pyrexia had continued so he was investigated to exclude malignancy this investigation proved negative Subsequently he was given 10 tablets of chloroquine and 12 injections of emetine and the pyrexia subsided His liver had remained enlarged and he had often had nausea and anorexia. He denied ever having had dysentery

*Examination*—The patient was well built, with no evidence of jaundice In the mornings he seemed well, but in the evenings his temperature rose to as high as 102 F and his pulse-rate to 100 per min. The respiratory cardiovascular and central nervous systems were normal The liver was enlarged down to the umbilicus and was firm smooth, and *not tender* The spleen was not *palpable*

*Investigations*—Blood: white cells 18,500 per c.mm (polymorphs 88% lymphocytes 12%) red cells 3,440 000 per c.mm.; Hb 10 g per 100 ml Erythrocyte-sedimentation rate 28 mm in first hour (Wintrobe) Urine investigations negative Fæces negative van den Bergh test negative; icteric index 4 units serum bilirubin 0 3 mg serum albumin 2 9 g serum globulin 2 75 g per 100 ml. Thymol turbidity 1 unit Alkaline phosphatase 5 units (Bodansky) Serum-cholesterol 150 mg per 100 ml Prothrombin time 30 sec (control 23 sec ) bleeding time 2 min clotting time 5 min platelets 370 000 per c.mm.

Fluoroscopy showed normal upper domes of the diaphragm and normal diaphragmatic movements Radiography after barium meal showed no abnormality of the stomach and duodenum Sigmoidoscopy revealed no abnormality up to 10 in Peritoneoscopy on Feb 5 to exclude malignancy of the liver showed diffuse enlargement of the right lobe of the liver up to the umbilicus the surface appeared smooth and there was definitely no evidence of malignancy or cirrhosis, the left lobe was also somewhat enlarged, the peritoneum seemed normal

*Treatment and Progress*—Amœbic abscess of the liver was tentatively diagnosed The patient was given emetine gr 1 and strychnine gr $^1/_{60}$ daily for ten days, but the pyrexia persisted Chloroquine to a total of 5 2 g was given over twelve days, but nausea and anorexia greatly increased and his condition deteriorated. On Feb 10 diagnostic aspiration of the liver yielded 30 ml. of greyish pus, which contained no amœbæ and was sterile on culture On the same day administration of aureomycin was begun with 500 mg intravenously, followed by 500 mg by mouth six-hourly A total of 20 g was given. The next day the temperature fell to normal, and it did not again rise The aureomycin rather than the aspiration must have been responsible for this dramatic improvement The patient's appetite also improved from the next day The liver, on the other hand, did not diminish appreciably in size, and drainage of the abscess was proposed But the patient felt so well that he requested his discharge, promising to return within a fortnight for the operation

*Readmission*—The patient returned on March 6 complaining that the previous night he had passed a dark stool and vomited a few ounces of partly clotted blood Blood white cells 10,000 per c mm (polymorphs 92%, lymphocytes 8%), red cells 3,780,000 per c mm., Hb 9 5 g per 100 ml The liver function tests were normal as before Liver biopsy on March 10 showed normal pattern The patient continued having tarry stools practically every day, with occasional hæmatemeses He was given one or more blood transfusions every day, according to the severity of bleeding, but his condition became very low On March 21, 1954, he was operated on.

*Drainage* (Mr M P Mehta)—The liver abscess was opened under local anæsthesia Greyish necrotic material and massive blood clots were evacuated. In view of the patient's feeble condition no further exploration was made A drainage tube was left in the abdomen Biopsy of the abscess cavity showed "fibrous tissue infiltrated by acute inflammatory cells No evidence of amœbic infection"

*Progress*—The abscess cavity continued to ooze blood in large quantities from the drainage tube, but the hæmatemesis and melæna stopped On March 26, however, he again had hæmatemesis and melæna and he was maintained mainly on blood transfusions By now the oozing from the wound had stopped. 36 transfusions were given in all On April 8, after the patient had bled for well over a month, laparotomy was done as a last resort

*Laparotomy* (Mr M P Mehta and Mr R J Maneckshah)—The stomach was distended The anterior surface of the first part of the duodenum was adherent to the liver After separation of the adhesions a large penetrating ulcer of the first part of the duodenum, about $1^1/_2$ in in diameter, was found to be penetrating the right lobe of the liver The ulcer was mobilised and buried, and a posterior gastro-enterostomy was done

*Progress*—Thereafter the patient improved, and in about four days melæna disappeared He was discharged on May 16, 1954 When he was last seen on Nov 3 the liver was not enlarged

## Discussion

Peptic ulcer as the cause of the bleeding was quite unforeseen, since repeated questioning had failed to elicit any previous history of hunger pain or dyspepsia, and radiography after a barium meal had been negative In any case, the patient's feeble condition militated against surgical operation—though laparotomy was eventually done as a last resort The massive blood-clots in the abscess cavity came from the ulcer, from which blood continued to ooze in large quantities through the drainage tube inserted into the abscess cavity

## Summary

A duodenal ulcer in a 58-year-old man penetrated the liver, causing hepatic abscess The patient also had hæmatemesis and melæna, but the diagnosis was in doubt until laparotomy was undertaken Recovery followed gastro enterostomy

I am grateful to the superintendent, B.D Petit Hospital, for permission to publish this case, and to Mr M P Meht and Mr R J Maneckshah for the operations

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# OPTIC ATROPHY AFTER ADMINISTRATION OF ISONIAZI WITH P.A.S

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We report the following case in the hope that any similar complaint will be treated with respect if it shoul be observed by a physician using isoniazid

The patient, now aged 35, was a prisoner of-war in Japanes hands for three and a half years, and had beriberi and righ foot drop On release his vision was normal and he had n ocular symptoms, but he was suspected to have pulmonar tuberculosis No evidence of activity was discovere till 1950, when his sputum became positive Cavitatio persisted in spite of sanatorium treatment, he refuse thoracoplasty

In 1953 a pneumoperitoneum was induced, and a course o streptomycin 1 g twice weekly and *p* aminosalicylic aci (P A.S) 20 g a day was given for two months There wa some improvement, and a further two month course of P.A.S 15 g a day and isoniazid 200 mg a day was started o Feb 2, 1954, as outpatient treatment Nine or ten day afterwards he developed a pain in the mid frontal area an noticed that his vision was becoming poorer The visua disturbance increased in severity, his vision reaching its lo ebb about March 25, just before the course of isoniazid an P.A S was completed

On April 8, 1954, when he was first sent to the eye depart ment of the Norfolk and Norwich Hospital his visual acuit was 2/60 in the right eye, and 6/60 in the left eye Correctio of the trifling refractive error made no significant improve ment He could not even read large type Both fundi wer normal, and the peripheral fields of vision were full Ther was no history to suggest any demyelinating disease, and n family history of Leber's optic atrophy or other hereditar type of degeneration The Wassermann reaction was negative, and the blood picture was normal Radiography of th skull showed no abnormality in the pituitary fossa or in th optic foramina Toxic neuritis due to nicotinic acid wa tentatively diagnosed

The patient was examined again on June 24, when bilatera optic atrophy had developed, but his visual acuity had no altered No other fundus changes were observed A genera medical examination revealed no associated neurological sign He has since been kept under continuous observation, bu no significant change in his vision has developed The disc now show a pearly white optic atrophy His standard o visual acuity is 4/60 in the right eye and 3/60 in the left With a telescopic lens for his right eye he can manage wit difficulty to read J6 in a good light

The significant feature here is that the patient notice deterioration in his vision about ten days after the cours of drugs had been started, and complained about it t one of us (P H S) Visual disturbance had not hithert been reported as a complication of this treatment, an his complaints were not considered to be relevant

The tolerance of P A S in the previous course o treatment, as well as the absence of reports that it i neurotoxic, seem to exculpate this drug There hav been frequent reports of toxic neuritis due to isoniazid, but not in the dosage used in the present case and neve of the optic nerves There therefore seems to be some idiosyncrasy present in this patient, because it seems unlikely that his past nutritional disease should be important at this late stage

We are indebted to Dr Kenneth Latter for the general examination of this patient

# POLIOMYELITIS NEONATORUM

W F Twining McMath
M.D Belf M R.C.P D P.H

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Paralytic poliomyelitis neonatorum is a rare disease Severin (1939) found that of some 18 000 recorded cases of poliomyelitis, only 22 began in the first month of life Shelokov and Weinstein (1951) cite Aycock as having seen a case in an infant only two days old Apparently the youngest patient referred to in the Bibliography of Infantile Paralysis (1951) is the 4-day old baby described by Frovig (1947)

> "The four members of one family having poliomyelitis during the same epidemic included a mother aged 20 and her newborn child The mother apparently acquired the disease in the last days of pregnancy the infant developed symptoms on the fourth day and four days later could not move arms, legs or head

In the following case symptoms of poliomyelitis appeared in a newborn infant at about the tenth day of life

On Sept 25 1954 a female infant aged 16 days was admitted to hospital for investigation The mother's pregnancy and delivery had been normal, and there had been no birth trauma The baby was breast fed and sucked well until the tenth day when the mother began to have great difficulty in waking her for feeds. This continued until the thirteenth day when the child was noticed to have paralysis of the left arm and shoulder

On admission the infant's temperature was 97 8°F The cerebrospinal fluid contained 100 lymphocytes per c.mm., 140 mg protein per 100 ml. and 35 mg sugar per 100 ml. White cells in the blood numbered 8000 per c.mm ; the differential count was normal. The infant had a complete flaccid paralysis of the flexors and extensors of the neck, of the left shoulder girdle and of the upper arm Paralysis of the wrist and hand was less complete With positioning and physiotherapy the movements of the wrist and hand improved, and the infant was subsequently transferred to an orthopædic unit.

Poliomyelitis virus, type I was cultured from the fæces of both the mother and the child

Although type I poliomyelitis virus was isolated from the fæces of the mother as well as of the child, the mother had experienced no symptoms that could be attributed to poliomyelitis

Most probably the contaminated fæces of the mother infected the child at the time of delivery Where symptoms develop two to four days after birth intra uterine infection should be suspected, since incubation periods of less than six days are uncommon Since infection can so easily occur during delivery, proof that intra uterine infection can take place will be forthcoming only when the virus has been recovered from a stillborn fœtus or from an undelivered fœtus in a patient who has died of poliomyelitis

The cerebrospinal fluid examination immediately before admission was carried out in Dr G Discombe's department at the Central Middlesex Hospital Dr A. P Goffe of the virus reference laboratory Colindale carried out the virus studies

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## Preliminary Communication

# TECHNIQUE FOR DEMONSTRATING NEUROSECRETORY MATERIAL IN THE HUMAN HYPOTHALAMUS

The theory that the posterior pituitary hormones are elaborated in the hypothalamus rests primarily on the demonstration in animals of an intensely staining material both in the cell bodies of neurones of the supraoptic nucleus and along their axones as they pass down the supraopticohypophyseal tract to the posterior lobe of the pituitary[1 2] This material was at first thought to represent the posterior pituitary hormones themselves, but is now widely regarded as a glyco lipo protein bearer substance for these hormones.[3–5] This view seems to be accepted by Barnett[6] who claims moreover to have shown by means of his dihydroxy dinaphthyl disulphide reaction for cystine that the posterior pituitary of some animals contains aggregations of a material probably consisting of the cystine rich oxytocic and antidiuretic octapeptides described by Du Vigneaud et al[7 8] and thus representing the posterior pituitary hormones

On the other hand there is evidence that the material demonstrated by Bargmann is not a bearer-substance, but that both in the hypothalamus and in the posterior

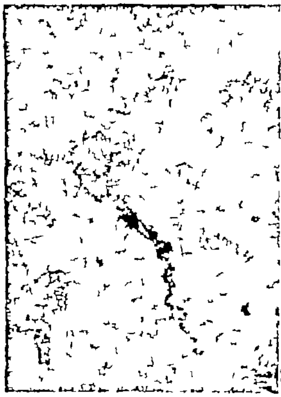

Fig 1—Cell-body and axone of neurone in paraventricular nucleus containing abundant neurosecretory material" (× 750)

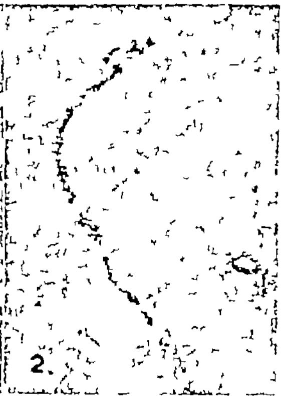

Fig 2—Beaded appearance of "neurosecretory material distributed along axone in region of paraventricular nucleus (× 750)

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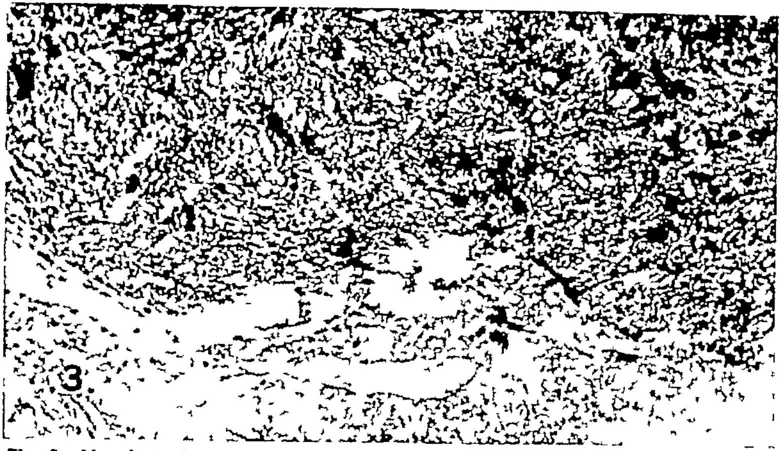

Fig 3—Abundant "neurosecretory material" in posterior lobe of pituitary, the anterior lobe lies below ( × 220)

pituitary, it is a protein or polypeptide rich in cystine—i.e , the hormone itself [9, 10] The histochemical technique on which this claim is based involves the reduction of ferric ferricyanide (Hardy,[11] modified by Adams [12]) and depends for its specificity on the fact that, with the appropriate controls, it reacts only with high concentrations of cystine , and there is some 19% of cystine in Du Vigneaud's octapeptides Consequently this technique has the advantage of demonstrating "neurosecretory material" but little else in the hypothalamus—a result which cannot be achieved with the far more sensitive technique employed by Barrnett, the application of which is of limited value in the hypothalamus

The ferric-ferricyanide technique thus provides the first adequate histochemical evidence of neurosecretion in the hypothalamus This, however, it achieves only in animals such as the cat and dog, in which there are large aggregations of "neurosecretory material" in the neurones of the supraoptic nuclei In man this material is less conspicuous , and, moreover, we found that existing staining methods were rather unsatisfactory because of their lack of specificity

### THE NEW TECHNIQUE

We have overcome these difficulties by devising a new technique capable of being applied to paraffin embedded formalin-fixed tissue This involves the oxidation of tissues by performic acid, and the subsequent demonstration of sulphonate radicles derived from cystine or cysteine with 'Alcian Blue' (Imperial Chemical Industries Ltd ) at pH 0 2 The reaction is intensified if preceded by the *immersion of the section in a reducing* agent—e g , sodium hydrosulphite

### MATERIAL

The human tissues examined by us were obtained at necropsies performed 4, 22, 41, 48, and 61 hours after death *The ages of the subjects (four males and one* female) were 55, 64, 35, 47, and 1

### RESULTS

In the human subjects, as well as in animals (including the dog) material throughout the neurohypophysis and in the supraoptic nuclei was stained a bright blue This reaction for reasons which will be published elsewhere we regard, with the appropriate controls, as an indication of a high content of cystine (or cysteine) Beyond occasional granules in the cell-bodies of other large neurones—e g , in the mamillary body—there was no similar material in the nervous tissue of the hypothalamus In the human subjects, the material was aggregated in the cell bodies of the neurones of the supraoptic and paraventricular nuclei, and spread down their axones (fig 1) , it was also present in the form of characteristic "beaded fibres" (fig 2) in the supraopticohypophyseal tract, and it filled the posterior lobe of the pituitary (fig 3)

Because of its distribution and high content of cystine, this material may reasonably be identified with posterior-pituitary hormone , its histochemical localisation in the human hypothalamus strongly confirms the hypothesis (hitherto based on the study of material from animals) that the posterior pituitary hormones are elaborated in the hypothalamus The performic acid alcian blue technique should therefore be of great value in the investigation of hypothalamic disturbances in man

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# Medical Societies

## ROYAL SOCIETY OF MEDICINE

### Toxoplasmosis

A JOINT meeting of the sections of pathology and comparative medicine was held on March 16 under the chairmanship of Prof L P GARROD, president of the pathology section

Prof CHRISTIAN SIIM (Copenhagen) described his experience of toxoplasmosis in Denmark He pointed out that it was easy for specimens from any part of that small country to be sent to the State Serum Institute, and it was also easy for the pathologist to see personally cases in any part of the country In the diagnosis of the disease, morphology alone was not to be relied on , attempts to isolate and maintain the toxoplasma by infecting mice often failed Serological tests were of great value in diagnosis , he used both the dye test and the complement fixation test Toxoplasmosis was widespread in the animal kingdom 10% of hares had been found to be infected with strains of toxoplasma identical with *those found in patients, and it occurred in other* species of animals The mode of spread was uncertain Food—for example, raw milk or raw meat—was an obvious possible route, and blood-sucking insects had also to be considered It was difficult to estimate the frequency of toxoplasmosis In some practices in Denmark 1 or 2 cases were recognised in every 2000 patients per year The disease appeared as congenital or acquired , and there were 3 clinical syndromes—lymphadenopathic, exanthematous, and encephalitic

Prof C P BEATTIE dealt mainly with epidemiology He mentioned a case of laboratory infection which he and his colleagues had recently reported, and he discussed other such cases, some fatal The epidemiology of toxoplasmosis had some peculiar features The parasite knew no boundaries of zoology or geography Infection could be transmitted through the placenta, yet it was difficult to infect mice by mouth Bites, skin scratches, and vaginal and tracheal mucous membranes seemed to be common avenues of infection Infection was rather common in veterinary surgeons and animal house attendants The picture was of a widely spread parasite which often reached a state of convenient symbiosis with a host human or animal and rarely caused serious trouble The mechanism of resistance to clinical infection was far from clear A mother might perhaps have come to terms with the parasite but the fœtus could be heavily infected as in congenital toxoplasmosis The presence of other disease sometimes seemed to activate the infection—for example in dogs suffering from distemper The rôle of antibodies was not clear—infection with toxoplasma did not necessarily cause disease

Dr I A B CATHIE discussed mainly laboratory diagnosis. Mouse passage was the most direct and in his hands had been a successful, method of diagnosis Other tests of value were the rabbit skin neutralisation test the toxoplasmin skin sensitivity test the dye test, and the complement-fixation test The last two were the most commonly used, but neither was entirely specific and they must be interpreted cautiously He regarded a serum titre of over 1/100 with the dye test together with a complement-fixation titre of over 1/8 as indicating probably an active infection Practically all the tests now used were done with Sabin's original strain of toxoplasma, and the validity of any tests in which this strain was used clearly depended on the correctness of Sabin's original identification of his strain as a toxoplasma

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# Reviews of Books

## Clinical Bacteriology

E. JOAN STOKES M B, M.R C.P clinical bacteriologist, University College Hospital London. London Edward Arnold 1955 Pp 288 20s

AFTER the decline of vaccine therapy diagnostic bacteriology was chiefly concerned with the detection of the specific fevers. Knowledge of bacteria and of the pathology of infectious disease increased without pause, but it was applied to preventive rather than to curative medicine. The hazards of the late war and the discovery of sulphonamides and the antibiotics have to some extent restored the importance of the subject, but it is still a neglected branch of clinical pathology too often regulated by rules of thumb (e g the words pathogenic ' and "saprophytic ) Meanwhile the current textbooks emphasise the systematic and epidemiological aspects of bacteriology rather than its relation to the diagnosis and cure of disease Dr Stokes s book is welcome because she assumes throughout that an accurate knowledge of the parasite and the reactions of the body to its presence is as important to the cure of the patient as it is to the progress of medicine This is a proper antidote to the not uncommon view that there is only one question for the bacteriologist to answer—to what antibiotic is the (unnamed) organism sensitive ?

The greater part of the book is devoted to the practical conduct of the bacteriological laboratory The subject allows no entirely logical arrangement and is considered both in relation to the specimen to be examined and the organism to be identified Few of the methods have not been published elsewhere (and there may be better ones than some of these) but this is the first time we believe that they have been set down in an orderly fashion between two covers and carrying the hallmark of personal experience Methods alone are of course not enough and there is much wisdom in the hints upon the interpretation of findings and the commoner pitfalls. We set the book several problems of a kind likely to arise in any laboratory and to each it offered a reasonable solution

Besides diagnostic bacteriology proper it includes sections upon other tasks which come to the hospital laboratory—the assay of antibiotics the testing of sterility and hospital epidemiology There are some omissions and very properly no mention is made of diseases alien to this country The section on mycology should be expanded or omitted There is a certain faddiness in method which experience will forget without loss. The advice on note-keeping may seem to aim high; but the recommended method is less formidable than it seems.

All in all this is the most valuable book for the clinical laboratory which has appeared for a long time and it is to be hoped that the introduction will not remain unread The failings of diagnostic bacteriology have not been those of method but of failure to realise the purpose, logic, and limitations of the methods Its results can seldom be stated in absolute numerical values of defined entities They are like the report of the histologist or the bedside diagnosis, personal opinions on complicated biological problems, based on observation and illuminated by experience The precepts of this book should go a long way to improve the shoddy standards, intellectual as well as technical which are obvious in only too many laboratories

## Clinical Physiology of the Lungs

CECIL K DRINKER M D D.SC formerly professor of physiology Harvard University School of Public Health, Boston, Mass Springfield Ill Charles C Thomas. Oxford: Blackwell Scientific Publications 1954 Pp 84 40s

## The Auxiliary Heart

WILLIAM WALTER WASSON M D Springfield Ill.: Charles C Thomas Oxford Blackwell Scientific Publications 1954 Pp 184 75s

IN both these monographs the authors are dealing chiefly with the pulmonary circulation and allied factors, such as elasticity of the lungs An analysis of blood flow through the lungs shows that the dynamics of the chest play a considerable part in maintaining the circulation For example the alteration in pleural pressure in respiration sucks blood into the great veins and acts as an accessory or auxiliary heart, and changes in pressure within the air passages referred to the pulmonary capillaries vary the flow Figures make clear the importance of this aspect of chest physiology For instance the 700 million air sacs have an alveolar surface of 50–100 square metres and in a normal-sized man between a tenth and a sixth of the blood volume is contained in the pulmonary arteries and veins. 3–6 litres passes through the lung capillaries each minute at rest but the figure may rise dramatically to 20 litres during hard exercise

Dr Drinker makes interesting observations on lung pathology showing how in emphysema the huge pulmonary reservoir can retain blood where the elasticity of the alveoli and capillaries has diminished The possibility that red blood-cells twist and bend to make their passage through the pulmonary capillaries may explain why with an obstruction to the lung circulation the cells may pile up and produce an infarct Dr Wasson points out that the failure of adequate diaphragmatic movement in the fat and elderly will produce shortness of breath, pain and cough which to some extent can be remedied by posturing the patient or by inducing a pneumoperitoneum so that the diaphragm is raised to a point of better advantage for respiratory excursion.

Both books are well illustrated and include some of Snow Miller s colour diagrams of the finer structure of the lungs. They are stimulating and valuable in emphasising the importance of an aspect of the circulation which is often overlooked

## Fluoridation as a Public Health Measure

Editor: JAMES H SHAW Harvard School of Dental Medicine Washington American Association for the Advancement of Science London Bailey Bros & Swinfen 1954. Pp 232 40s

THIS is the third symposium in a series. The two earlier ones dealt with the natural presence of fluorine in water and described how in excess it may have a toxic effect and how in small amounts it may reduce dental caries. This third volume discusses the purposeful addition of fluorine to public water-supplies, and its 21 contributors are bound together by their common zeal for fluoridation It appears in the middle of the controversy which crossed the Atlantic in the wake of the United Kingdom mission and its 450-odd references offer scope for further reading To the converted it will provide useful ammunition to the doubters it may seem a little biased; to the opponents of fluoridation may look like an attempt to blind with Science

There is an interesting evaluation of vehicles other than the public water-supplies for administering fluorine to the small group of the community that need it, and a frank admission that little is known on this point, so the contentious technique of mass medication may yet be avoided by some form of voluntary dosage. The book deals with fluorine phenomena as purely scientific and engineering experiments and observations, and as such deserves respect, but the fluoridation of public water-supplies raises ethical and human problems which are not given due weight. Perhaps the next volume in the series will restore the balance.

**The Development of Tropical and Subtropical Countries**

*With particular reference to Africa*. Editor A. LESLIE BANKS, M.A., M.D., F.R.C.P., D.P.H., barrister at law, professor of human ecology, University of Cambridge. London: Edward Arnold. 1955. Pp. 217. 18s.

TWO years ago, with the help of the Rockefeller Foundation, Professor Banks invited a group of 32 agriculturalists, economists, educationalists, doctors, and sociologists to visit Cambridge to discuss general problems of African development and especially the importance of power and water, food and its production, health and welfare, and education. This book is a transcript of a mechanical recording of the discussions, after each contributor had made corrections. The subjects were well chosen and, as the speakers for the most part showed both knowledge and imagination, the book is lively reading. Its appeal is broad and experts in a great variety of techniques can learn from it, and the medical reader may be surprised to find how intimately the practice of curative and preventive medicine in Africa is bound up with other disciplines.

But a transcript of a symposium is never wholly satisfactory, and this one is often disjointed, seldom properly documented, and occasionally nonsense. Is it too much to hope that Professor Banks will find time over the next five years to digest and expand the excellent material collected here and give us a coherent and well documented monograph?

**Chemistry and Biology of Pteridines**

*A Ciba Foundation Symposium*. Editors G. E. W. WOLSTENHOLME, O.B.E., M.A., M.B., MARGARET P. CAMERON, M.A., A.B.L.S. London: J. & A. Churchill. 1954. Pp. 425. 42s.

THE pteridines are related to the purines in that the basic pteridine ring system contains one more carbon atom than that of the purine molecule. Pteridines were first discovered, some sixty-five years ago, by Sir Frederick Gowland Hopkins as pigments of butterfly wings; since then they have been found widely distributed in nature in pigments, in the vitamin folic acid, and in other forms.

The first part of this symposium, on the chemistry of pteridines, provides a lucid account of an interesting branch of heterocyclic chemistry. In the second part, which deals with the biology of pteridines, Dr. D. D. Woods gives an account of the relation of *p*-aminobenzoic acid (a sulphonamide antagonist, and constituent of the folic acid molecule) to folic acid in micro-organisms. Three papers are concerned with the effect of pteridines in man. Dr. W. Jacobson describes the effect of the folic acid antagonist, aminopterin, on mitosis of cells in leukæmia; Dr. R. H. Girdwood discusses the relation of disorders of folic acid metabolism to anæmias; and Dr. Jacob Colsky deals with hepatic cirrhosis in children suffering from leukæmia and treated with aminopterin and amethopterin. The emphasis is chiefly on the fundamental nature and biological action of this interesting class of compounds.

**Adrenal Cortex.**—The Josiah Macy, jun., Foundation, New York, has published the transactions of the conference on this subject held in November, 1953. The editor is Dr. Elaine P. Ralli. (1954. Pp. 187. $3.75.)

# New Inventions

## AN INSTRUMENT FOR DIVIDING FLEXOR RETINACULUM

ACROPARÆSTHESIÆ involving the thumb and lateral two fingers of the hand may result from a lesion of the median nerve at the wrist—the "carpal-tunnel syndrome." McArdle[1] first attributed these acroparæsthesiæ to compression of the nerve as it runs from the wrist to the palm beneath the flexor retinaculum, and Kremer et al.[2] showed that incision of the retinaculum, by releasing the compression of the nerve, gave immediate and permanent relief of pain in most cases.

In the open operation an incision is made along the medial border of the thenar eminence up to the wrist and then transversely across the wrist. The retinaculum is divided under direct vision, and the median nerve inspected for pathological changes. The healing of such a wound leaves much to be desired: the scar is usually raised and tender, and may become adherent to the median nerve, with subsequent pain on movement of the hand.

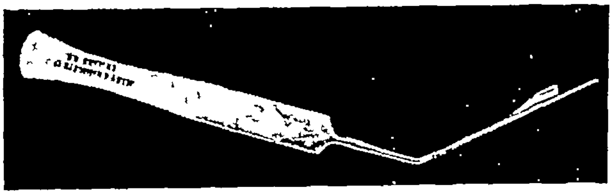

Fig. 1—Lateral view of retinaculotome.

The closed operation is done through a small transverse incision at the wrist. The retinaculum is opened under direct vision and an instrument—usually a bistoury—is inserted beneath its fibres to divide the ligament from the wrist to the palm. In the process of cutting the ligament the bistoury must, because of the depth of its blade, press heavily upon the median nerve, thus aggravating the condition which the operation is designed to relieve; and matters are made still worse if a guard (such as a Macdonald's dissector) is inserted beneath the bistoury.

To avoid such a danger I have designed the instrument shown in the accompanying figures. It consists essentially of a base-plate upon which, at right-angles, is set the knife-blade. The base-plate is $2^1/_4$ in. × $^1/_4$ in., a size that usually allows it to pass easily through the carpal tunnel. The handle of the base-plate is flat and set in the same plane as the knife, so that the operator can always tell the position of the knife edge. The knife itself is set $^1/_2$ in. back from the end of the base-plate to ensure that the cut will be made along the line of the median nerve. The knife-blade is triangular; the small cutting side is only $^1/_8$ in. high and has a slightly concave border. The back of the blade is rounded to prevent damage to the overlying tissues. The retinaculotome cuts more readily if the incision of the ligament is begun with a pair of scissors. The blade should be kept very sharp with a small emery stone.

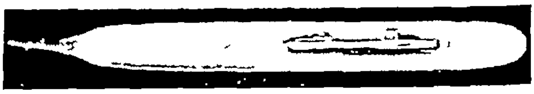

Fig. 2—Base-plate of retinaculotome, from above.

I have used the instrument in 15 cases without any difficulty or mishap. The immediate results of operation are as good as with conventional methods of dividing the ligament. Where the carpal tunnel is exceedingly narrow the instrument cannot be used, but in these circumstances the blind operation cannot be performed by any other method, and one must resort to the open operation.

The retinaculotome was made for me by Messrs. Allen & Hanburys, London.

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[1] McArdle, M. J. Communication to the Association of British Neurologists, October, 1951.

[2] Kremer, M., Gilliatt, R. W., Golding, J. S. R., Wilson, T. G. *Lancet*, 1953, ii, 590.

THE LANCET

*LONDON SATURDAY, MARCH 26 1955*

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## Nutrition and Anæmia

It has long been suspected that relative deficiency of some food factors plays a part in the ætiology of anæmia in apparently well fed patients, and it is this suspicion that causes some physicians to treat patients with "blunderbuss" remedies containing various metals, vitamins of the B group, protein digests and fractions and so on. Hæmatologists deprecate such polypharmacy, which runs counter to the considerable body of firm information about essential factors in the management of anæmia. Much of this information is well summarised in a symposium published in the *American Journal of Clinical Nutrition*.[1]

A substance may be a limiting factor in blood formation if it is not synthesised in the body, is not readily accessible to the bone marrow, or tends to be affected by disturbances of absorption in the alimentary tract. The only truly essential hæmatinics whose supply is liable to be limited in one of these ways are iron for hæmoglobin formation and vitamin $B_{12}$ and folic acid for nucleic acid synthesis; so far as we know other substances are so readily available that they are never limiting factors. Judged by number of patients, iron deficiency is by far the most important cause, and on this Prof. CARL V. MOORE[2] makes some important observations. He and his co-workers have circumvented the difficulties of balance experiments by incorporating radioactive iron into various foods. Thus radioactive iron was injected into hens and then their flesh, their livers, and their eggs contained the isotope; similarly vegetables were grown in nutrient solution containing radioactive iron. Such marked foodstuffs were used to prepare ordinary dishes and were fed to healthy people and to patients with iron-deficiency anæmia. The results show that with few exceptions, the proportion of iron in food that is normally absorbed is 10% or less; the only two persons who absorbed more than 10% had been given chicken muscle. Iron-deficient patients only sometimes absorbed more than 10% from eggs, but they more often exceeded this level if chicken liver, vegetables, and yeast were given. An important finding was that ascorbic acid usually increases the assimilation of iron from food and that this property is shared by some, but not all, reducing substances. The addition of hydrochloric acid to the stomach of patients with hypochlorhydria did not improve their iron absorption. These points are brought out in a study by STEINKAMP et al.[3] undertaken to see whether iron salts used to "fortify" bread would be absorbed in large enough amounts to make the addition worth while. For industrial reasons ferric orthophosphate and reduced iron powder are used more often than ferrous sulphate; sodium ferric pyrophosphate has also been used. To the investigators' surprise these four forms of iron were equally effective when baked into bread, whereas in the free form ferrous sulphate was better absorbed than the others. Healthy people absorbed 1–12% of the iron given in the bread, iron-deficient patients absorbed 45–64% of the iron, and four people apparently healthy but suspected of having low iron stores absorbed 26–38% of the $Fe^{59}$ used. MOORE states that the normal adult diet in the U.S.A. contains about 12–15 mg. of iron a day, so the amount absorbed from food is somewhere between 0·6 and 1·5 mg. daily. The amount will be less with poor diet, infection, diarrhœa, or steatorrhœa, and possibly greater in patients with iron deficiency. MOORE and his colleagues have also worked on the excretion of iron in desquamated skin cells, sweat, and urine, and calculate that the daily loss of iron is about 1 mg. These figures show how precarious is the iron balance of the healthy woman during her menstrual phase of life and during pregnancy. The volume of menstrual blood is 35–70 ml., at 12 g. hæmoglobin per 100 ml. of blood this means a loss of 14–28 mg. of iron—or 0·5–1·0 mg. a day over a twenty-eight-day cycle. During pregnancy the mother provides for her baby some 300–500 mg. of iron, or 1–2 mg. a day. Thus with not more than 1·5 mg. a day coming in from food, and up to 1 mg. a day excreted by regular channels, it requires only a poor diet or a little extra menstrual loss to cause a negative balance and eventual iron-deficiency anæmia. The pregnant woman is almost certain to lose some iron during the nine months' gestation. It is not surprising then that iron-deficiency anæmia is so common in these two groups of women. In men or in post-menopausal women iron deficiency is much less likely to develop unless there is some loss of blood. MOORE takes two hypothetical examples—a man with a hæmoglobin level of 15 g. per 100 ml. and a blood volume of 5 litres, and a woman with a hæmoglobin level of 14 g. per 100 ml. and a blood volume of 4 litres—and he calculates that if these persons absorbed no iron at all and continued to excrete 1 mg. a day it would take six years in the man and four years in the woman before the hæmoglobin fell to 7·5 mg. per 100 ml. (50%). These times would certainly be longer in reality, because iron-deficient patients excrete less iron and any iron in the diet tends to be absorbed more efficiently unless the small-intestine mechanism is abnormal. So MOORE concludes that, though it is theoretically possible for iron-deficiency anæmia in men and post-menopausal women to be purely nutritional, sources of blood loss should be very carefully sought.

It has been often asserted that the absorption of iron may be helped by the addition of traces of metals—particularly copper, cobalt, molybdenum, and zinc. This question has been investigated by CARTWRIGHT.[4] He concludes that there is no evidence that either molybdenum or zinc have the slightest effect. Copper is in a different class. An anæmia of swine is traceable to copper deficiency, and CARTWRIGHT describes evidence that copper plays an important part in the absorption and utilisation of iron and its movement from iron stores. But this does not mean that any anæmic patient needs to be given copper. In fact it is very difficult to find a diet that does not contain an excess of copper; the newborn infant has large copper stores, and inorganic-iron preparations all contain traces of copper that are more than sufficient So CARTWRIGHT, citing the dictum that " all unnecessary therapy should be avoided," advises against the administration of copper to patients (It is just possible that some patients with sprue or the nephrotic syndrome may not absorb enough copper, but this is unproved ) Cobalt is known to have a definite effect on erythropoiesis, apart from the fact that it is present in the molecule of vitamin $B_{12}$ Cobalt-deficiency anæmia is recognised in ruminants, but this anæmia is now known to be due to deficiency of vitamin $B_{12}$ Administration of cobalt in relatively large amounts causes true polycythæmia in some animals and birds, with hyperplasia of red-cell-forming tissues, but this seems to be a toxic rather than a physiological effect CARTWRIGHT points out that in man 5 µg of cobalt is all that is needed daily, and probably much less suffices , clinical deficiency of cobalt per se has never been recognised There is good evidence that administration of cobalt over a long period raises the hæmoglobin level in anæmia secondary to infection, malignant disease, and renal disease , this action is probably pharmacological, and there are many unpleasant side-effects CARTWRIGHT does not think that there is any proof that cobalt aids the absorption of iron, and he is not convinced of its value in aplastic anæmia and chronic hæmolytic anæmia (But Dr FOUNTAIN and Dr DALES [5] have lately described in these columns a case of pure red-cell aplasia in which other measures had failed and complete recovery followed administration of cobalt )

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[1] Symposium: nutritional aspects of blood formation. *Amer. J. clin. Nutr.* 1955, 3, no. 1.

[2] Moore, C. V. *Ibid*, p. 3.

[3] Steinkamp, R., Dubach, R., Moore, C. V. *Arch. intern. Med.* 1955, 95, 191.

[4] Cartwright, G. E. *Amer. J. clin. Nutr.* 1955, 3, 11.

MUELLER and WILL [6] have examined the relations between vitamin $B_{12}$, folic acid, and ascorbic acid in megaloblastic anæmia They agree that vitamin $B_{12}$ and folic acid act as catalysts in the formation of nucleic acid, and that ascorbic acid has an indirect effect on folic acid metabolism It has to be also assumed that vitamin $B_{12}$ is in some way connected with folic-acid metabolism, since deficiency of vitamin $B_{12}$ causes a conditioned deficiency of folic acid Folic acid, they consider, produces temporary remission in pernicious anæmia by a mass action effect, mobilising the depleted vitamin-$B_{12}$ store and thus paving the way for a worse relapse with aggravation of neurological disturbances MUELLER and WILL point out that vitamin $B_{12}$ can be bound and utilised locally by erythropoietic cells and will cause them to mature, whereas folic acid has no such direct action Folic acid acts at some other point in the biochemical synthesis of nucleoprotein , megaloblastic anæmia of pregnancy, for example, may be a conditioned deficiency of folinic acid co enzyme Our therapeutic use of vitamin $B_{12}$ is influenced by the fact that intrinsic factor, secreted in man in the upper part of the stomach, is essential for its absorption from the small intestine SCHILLING [7] estimates the daily requirement of vitamin $B_{12}$ at less than 1 µg , for therapy we usually give ten times this amount, by intramuscular injection or as nasal " snuff " VILTER [8] does not recommend the combinations of $B_{12}$ with intrinsic factor that can be given orally , they are not equally effective in all patients and are relatively expensive

This symposium closely supports with scientific evidence what is generally regarded as good clinical practice—namely, to treat iron-deficiency anæmias with simple iron preparations that include no added trace metals, vitamin-B complex, and so on, and to give ascorbic acid with the iron , to treat pernicious anæmia with vitamin $B_{12}$, and the megaloblastic anæmias of pregnancy and steatorrhœa with folic acid , and never to give folic acid to patients with proved or suspected pernicious anæmia

## Clonal Ageing

THREE impressive lectures on the genetics of paramecium were recently delivered at University College, London, by Prof TRACY SONNEBORN, of the University of Indiana Although their subject was specialised, they included much to interest medical as well as general biologists Among much important new information on ciliate genetics, SONNEBORN gave a convincing experimental analysis of the reason why stocks of paramecium invariably deteriorate unless they are sexually renewed This organism shows very well the phenomenon of " clonal ageing ", and SONNEBORN's work explains the process in this instance Unfortunately for those who work on mammalian ageing, the reasons are probably peculiar to paramecium , but they raise a great many points of fundamental importance in cytology

The so called ageing of clones bulked large in the minds of biologists in the 1890s when they considered senescence in higher organisms and man A clone comprises all the cells produced by simple asexual fission from a given sexually produced nucleus A variety of strawberry or of Russell lupin provides a familiar example the original plant was a hybrid produced by the fusion of two gametes and grown from seed, and all its descendants produced by cuttings or by division of the original root stock constitute a clone All the asexually produced descendants of a protozoan which has just undergone one of its characteristic sexual processes—conjugation, autogamy, pædogamy, and so forth—make up a clone So, in a different sense, do the cells of a metazoan body, for they all arise by simple fission from one sexually produced nucleus It was early observed that while some protozoans could apparently be maintained indefinitely by simple fission alone, others soon lost vigour and died if they were not permitted to undergo periodic sexual phases WEISMANN had held that the germ-plasm was immortal and the soma destined to die , might it not be that the ageing of the metazoan body, and the loss of vigour in clones, arose from the same source—the necessity for periodic sexual reorganisation as a condition of continued vigour ? MAUPAS propounded this idea , and for many years a vigorous competition was conducted between protozoologists in seeing how many asexual generations of paramecium, eudorina, and similar creatures they could rear In the course of this process much nonsense was written about " potential immortality," but a great deal was learnt about protozoan reproduction and culture methods It became evident that some clones deteriorate and others, including somatic cells such as fibroblasts in tissue-culture, do not The results obtained by the gardeners were similar—there are plants which can be grown indefinitely from cuttings, and others which lose thrift unless they are periodically regrown from seed The possibility that one important kind of body cell might undergo progressive loss of vigour or progressively more inaccurate copying the further it gets from the germ line, still remains for the gerontologist Some plant clones deteriorate because they accumulate viruses, others fail with striking unanimity after a given period, whole plantations being simultaneously affected even when they are widely separated A clonal degeneration of this kind ("June yellows" in strawberries) has lately been shown[1] to be a true degeneration of a particular genetic interest Apart from this example, which is being investigated, the mechanisms involved in the decay of any of the susceptible cell lines have not hitherto been established

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[5] Fountain J R Dales M. *Lancet* March 12 1955 p 541
[6] Mueller J F Will J J *Amer J clin Nutr* 1955 3 30
[7] Schilling R F *Ibid* p 45
[8] Vilter R W *Ibid*, p 72

The mechanism which SONNEBORN finds has been suggested[2] but has never previously been demonstrated When paramecium divides after a sexual process, the new nucleus of each daughter cell divides into two One of these products, the micronucleus which reaches the anterior end of the cell has the normal diploid number of chromosomes and is apparently concerned solely with conveying the genotype it is, in other words the germ plasm' The other portion the macronucleus, controls the metabolism of the cell It becomes highly polyploid, and at subsequent cell divisions while the micronucleus divides evenly in the normal manner of nuclei, the macronucleus distributes its chromosomes at random to the daughter macronucleus arising from it Because of the enormous number of sets which it contains, every cell in the earlier divisions has a fair chance of getting its quota, but with the passage of time more and more daughters receive an unbalanced set and a reduced physiological repertoire and a chromosome once lost cannot be restored from the micronucleus except by sexual division—conjugation or autogamy In the later stages of clonal senescence en sexual division is affected and abnormal or non able products increase SONNEBORN has shown that is is not due to the accumulation of mutations since can be prevented by periodic autogamy even ough this does not alter the genotype it appears be due to injury inflicted upon the micronucleus self through the abnormal intracellular conditions roduced by the defective macronucleus In ciliates e germ plasm has to live in the cell where the rocesses of somatic maintenance are carried out, and is therefore unusually exposed This is probably a nique situation—it does not even apply in other iliates—and the division of function between vege ative and germinal nuclei is confined to this group ut it does not follow that this type of clonal ageing as no bearing at all on senescence in higher animals Ve do not know whether faulty copying and aneu loidy in somatic cells (which would be the rough quivalent of macronuclear degeneration in paraecium) help to determine the life-span of metazoa omatic aneuploidy though it has been described,[3–5] s not a popular concept with cytologists, it is easily imulated by bad technique[6] If it does occur in any important tissue, senescence, or some other adverse process such as malignancy, might well result from it Furthermore we do not know exactly the extent to which somatic senescence can produce chromosomal damage in germ cells Parental age effects are familiar, but in most of these, cytoplasmic factors appear to predominate and the consequences are not as a rule genetically fixed. The real importance of Professor SONNEBORN's work, as revealed in his lectures, lies in the information about the fine structure of intracellular physiology which he has obtained by simple but highly ingenious methods This approach has proved brilliantly successful not because paramecium is a 'good" organism, but because it has been studied by a good biologist Its intracellular homoeostatic systems are at least as complex, it seems, as the gross homoeostatic mechanisms of man or dog This is an alarming thought, but at least Professor SONNEBORN has shown how they can be approached

# Annotations

## FIRST AID TREATMENT OF HEAD INJURIES

MANY of us have seen the unconscious motor cyclist lying on the road while people gather round and warn each other not to move him because ignorant manoeuvres might do harm Thus the unfortunate victim lies in a huddle until an ambulance arrives with its staff trained in first-aid. For what happens next we must turn to the first aid manuals and we at once realise that these give instruction which ignores modern knowledge regarding the causes of death after head injury the grave dangers of inhalation asphyxia in the unconscious patient have not yet filtered into these manuals

After head injury vomiting is common and the inhalation of gastric juices may lead to death a few hours after the inhalation has taken place Yet one first aid manual advises for fracture of the skull 'Lay the patient on his back in all cases keep his head and shoulders raised and support them on a pillow or a rolled up blanket Again in the first aid treatment of insensibility Lay the patient on his back These instructions are acted on throughout the country, even though they ignore the dangers of inhalation of blood and vomit On the other hand a leaflet on the Early Treatment of Head Injuries lately published by the advisory committee in neurology and neurosurgery to the North East Metropolitan Regional Hospital Board declares *the patient should be kept on his side with a clear airway* This advice is intended for doctors and nurses but it is even more important that it should be acted on before the patient reaches hospital when perhaps blood is flowing into the pharynx from a *fractured base of skull*

There are some hazards in encouraging first aid workers with regard to postural drainage of the throat and lungs for multiple injuries may be present but this difficulty is not insurmountable and the present advice is so dangerous when the patient is deeply unconscious that those concerned with first aid instruction should review the matter without delay The first aid worker could at least be taught to listen to the patient's breathing and if there is a death rattle" in the throat to establish postural drainage whatever the risks In such cases it is essential that postural drainage of the air passages be maintained in the ambulance on the *hospital trolley*, and in the X ray department as well as in the hospital bed in the same way as with patients who have bulbar paralysis due, say, to poliomyelitis

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[1] McWhirter G In the press.
[2] Fauré Frémiet E *Rev suisse Zool* 1953 60 426
[3] Hsu T C, Pomerat C M *J Morph* 1953 93 301
[4] Tanaka, T *Cytologia Tokyo* 1953 18, 343.
[5] Sorokina M I. *Bull Acad Sci U.R.S.S* 1950 6, 97
[6] Walker B E, Boothroyd E R. *Genetics* 1953 39 210

## BACKWARD IN READING

LIKE a particle dropped into a supersaturated solution, even a small disability can act as a nucleus round which other things crystallise Learning to read is not essential for survival and no instinct is satisfied by the power to distinguish written symbols in fact man got along without this skill for more than a couple of million years, and other animals still do Yet so high is the value we set on it in Western civilisation that the child who fails to read by the "proper" age (arbitrarily fixed at 6–7) is an object of concern to his family and shame to himself His difficulties, it is believed, may be due to crossed laterality—a personal peculiarity which does not seem to hinder his performance in any other direction Pearce,[1] who studied the lateral preferences of a group of healthy school-children, found complete right sided dominance in only 49% , complete left sided dominance was much rarer, only 4% of the children showing it , the remaining 47% had one or two organs—eye, ear, hand, or leg—out of step Nearly three-quarters of those with schooling difficulties belonged to the crossed lateral group , and those with specific reading difficulties had one basic symptom—they tended to reverse the order of letters as they read them The left eyed child finds it natural to scan a line of type from right to left , he may meet our arbitrary demand that he should read from left to right by unintentionally swapping a letter round from time to time If the letters are arranged vertically, it seems, they give him no trouble A child with this tendency to see letters transposed will inevitably take longer to learn to read than others, especially if he is not bright enough to overcome the difficulty by himself The dismay of his parents and teachers and derision of his clever little friends can be very damaging to his self esteem, and if he failed to call out defences he would be a very abnormal child indeed

Downes and Schuman [2] report some of the forms these defences may take The most obvious thing about him is that he hates being made to read and may panic or stammer if he is given a reading test Other distress signals, they note, are "knee-jerking, nail-biting, paper tearing, face fussing, hair pulling (both his own and that of other students)" Again, he may use bad language, cheat, steal, destroy property, or bully , or he may determine to excel in other directions—captaining a team, taking up a hobby, or making himself popular with the girls At home he does anything but read, preferring radio, television, bird watching, telephoning his friends, or even helping with the washing up He will never write a letter He plays with younger children and prefers the company of "the maid, the handyman, and the not-so nice children down the block" His sense of being different, of having a gap in his faculties, may be very alarming to him "there seems to be a deep seated, pervasive, terrifying kind of disunity in the world of the disabled reader" He tends to be emotionally immature, and knows it , and his schoolmates know it Feeling inadequate, and lacking expert help in overcoming his difficulty, he may become deeply discouraged "he comes to equate good reading, school success and high marks with parental approval and love" This anxiety for approval may be transferred in later life to his employer or to society He may become a perfectionist, unwilling to risk a mistake , and his dread of making one may limit more and more the field in which he dare trust himself Such a child makes no trouble for parent or teacher "he finally never makes any trouble, or anything else for that matter"

It is unfortunate that such a mild and common deviation from the usual pattern should be allowed to become the centre for a host of disabilities A better understanding of the causes of backwardness in reading, and more skilled management of those who display it, might save much unnecessary trouble both for teachers and taught Reading disabilities are not uncommon Downes and Schuman estimate that 12–15% of boys and half that proportion of girls show them It seems worth trying to discover these children early and give them the kind of help they need

## PSYCHIATRIC EVIDENCE IN MURDER TRIALS

BETWEEN 1900 and 1949 more persons in the United Kingdom accused of murder were sent to Broadmoor than were executed , and in considerably more than half the murder trials in England and Wales the question of the accused person's sanity is debated in court It might therefore be expected that the evidence of doctors with experience of mental disease would carry much weight in such trials Some of the reasons why this is by no means invariably so were considered by Dr J A Hobson at a meeting of the Howard League for Penal Reform on March 16

The excuse that psychiatry is a new subject and that the courts, being conservative, are reluctant to accept its teachings can, said Dr Hobson, hardly be maintained , for, although the term psychiatry was not introduced until a few years after the McNaughten trial, specialists in mental disease were giving evidence in murder trials long before that date The main cause of the resentment felt by the legal profession for the psychiatrist's evidence was that he was trying to usurp the domain of the lawyer when he gave evidence about mental happenings, motives, or antisocial behaviour The suspicion that the psychiatrist was biased was no new thing in English courts of law the Lord Chancellor in 1862 stated that "the introduction of medical opinions and medical theories into this subject [the criminal law] has proceeded upon the vicious principle of considering insanity as a disease" The fact that in English criminal courts witnesses were called either by the prosecution or the defence, and that there was no machinery for bringing before the court the evidence independently, at once suggested bias The conflict between the psychiatric witnesses on the two sides was often more apparent than real, but court procedure emphasised any differences It sometimes became the duty of the opposing counsel deliberately to make differences seem as wide as possible, and journalists in reporting sensational murder trials exaggerated still further any differences of opinion

The psychiatric witness in a murder trial is anxious to say all that can possibly be said on behalf of the accused, and this is sometimes regarded as bias Dr Hobson suggested that it was in keeping with the general principles of English criminal law that the psychiatrist should be biased in this way, whether he gave evidence for prosecution or for defence Sometimes not all the facts in the psychiatrist's report were brought out in evidence, since they might be deleterious to one or other side, and this resulted in the court not being given all the information available Dr Hobson agreed with Dr Desmond Curran's opinion[1] that bad psychiatric evidence was being called too often, and that the procedure for calling psychiatric evidence was largely responsible for this—in other words, that the legal profession was as much to blame as were the doctors There were three principal causes for this unsatisfactory state of affairs

1 Solicitors select psychiatric witnesses by going from one psychiatrist to another until they find someone willing to give an opinion favourable to their client If two or three experienced psychiatrists cannot find anything helpful to say, any psychiatrist who will say more will probably be either less skilled or less honest

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[1] Pearce R. A H *Arch Dis Childh* 1953, 28, 247 , see also *Lancet*, 1954 i 141

[2] Downes M G , Schuman, R S *New Engl J Med* 1955, [illegible]

[1] Curran D *In* The Roots of Crime Edited by Sir Norwood East London, 1954

2 Good psychiatric evidence is not always available, since any first-rank psychiatrists will not take court cases The me and trouble involved and the risks of unfavourable ublicity resulting in loss of professional prestige make many ychiatrists chary of undertaking such work Dr Hobson marked that the provisions made for compensating psychi ric witnesses in legal aid cases were most inadequate the pular belief that there were large rewards for the forensic ychiatric expert was quite unfounded. Proper examination volved several interviews. In addition he usually found it cessary to make inquiries outside the prison, visiting the isoner's home interviewing relatives and workmates and metimes arranging with the police for further investigations be made It was always necessary in addition to have a nsultation with solicitors and counsel

3 Psychiatric evidence is also sometimes bad because it is ven in psychiatric rather than in legal language It is not ufficiently realised that there are three languages spoken in ourt that of the psychiatrist or other medical expert legal nguage and the layman's language According to Mayer ross et al [1]: The medical witness is embarrassed by his capacity to put highly relevant facts about the state of mind f the accused. The debate centres around not the medical cts, but metaphysical issues of which if they have a meaning t all, the medical man has no direct knowledge The language s alien to him He is likely to be asked to give yes or no nswers, although he knows full well that he cannot in most ases be dogmatic, and that in fairness to himself and to the ourt he should explain the significance of his replies to the ase at issue.

The McNaughten rules had been criticised so often for heir divorce from reality their illogical metaphysical asis, and the inequality with which they were applied hat it would be repetitious to discuss them further Dr Hobson felt that they were a serious barrier to the development of understanding between psychiatrist and lawyer and that they impeded the lawyer's understanding of the facts of mental illness He agreed with Mayer Gross et al : Psychiatric evidence in English courts will not be measured by a realistic yardstick until the M'Naghten Rules are abolished altogether" but he did not think that Mayer Gross went far enough He himself preferred the view of Overholser [2] Capital punishment has no place in the modern scheme of penal treatment and if capital punishment were abolished nearly all of the public furor against expert psychiatric testimony would disappear' *Not only would the furor disappear* but there would be very little need of expert psychiatric testimony When capital punishment was abolished the psychiatrist would seldom be called on to give evidence and when he did so he would at last be able to talk sense instead *of psycho legal nonsense*

## CALCIUM DEPOSITS IN THE HAND

SUDDEN acute pain in the hand is usually due to infection or injury Carroll et al.[3] draw attention to one of the less common causes—namely calcium deposits In most of their cases the patient sought attention soon after the onset of pain cradling a swollen and tender hand The wrist and digits were flexed and immobile and there were tender spots around the wrist or in the region of the finger joints. Radiographs of the most tender areas showed calcium deposits these deposits were often small and in the region of the carpus special projections were necessary to display them The deposits lay within the muscles and ligaments most commonly in the flexor carpi ulnaris in the region of the pisiform bone If the deposit was surgically exposed it appeared as a creamy material beneath œdematous and inflamed peritendon or ligament There is no evidence that trauma plays any direct part in the production of such deposits and although some patients had similar deposits in other regions there was no very clear metabolic factor Radiography showed that calcium deposits might be confused with chip fractures accessory bones, or small bony deposits due to periosteal tears. The deposits were temporary the disease was acute, severe and brief and without treatment the pain subsided within three weeks The radiographic shadows commonly disappeared even sooner: the average time before disappearance was two weeks. No deposit persisted for as long as six months Local injection of procaine relieved the symptoms, and surgical evacuation of the deposit seemed rarely to be indicated

Diagnosis of this disorder should not be difficult Differential diagnosis from minor fractures may present problems, but the more widespread disturbance and the more severe pain from the calcium deposit should be valuable guides. Clearly the final proof is radiographic and the early disappearance of these deposits confirms their nature

## TUBERCULIN TESTS

THE W.H O Tuberculosis Research Office has continued its investigation of the prevalence and cause of low grade tuberculin sensitivity in man [1] The differences in the patterns of sensitivity have now been studied in twelve countries, from Denmark England, and the U S.A to Ethiopia the Philippines, and Viet Nam The greater the response to large doses of tuberculin in those insensitive to smaller ones, the more the reactions to the small doses tend to fall within the 6–12 mm. range and the more the frequency-distribution resembles the normal curve with a clear demarcation between the group with large and the group with very small or no reactions If it is assumed that only the normally distributed portion of the curve represents infection with tubercle bacilli the proportions of infected in the different countries can be approximately estimated Among school-children this proportion was found to vary from nearly 50% in the Sudan to 4% in the White population of the U.S.A and a little under 10% in this country From further assumptions—supported by other observations—it can be calculated that non tuberculous tuberculin sensitivity occurs in over 90% of school-children in the Philippines Viet Nam and the Sudan 70–80% in India, about 50% in Ethiopia and Turkey, 20–30% in England and Mexico and under 10% in Denmark and the southern part of the U S.A The practical implication of these investigations if the hypothesis of non tuberculous reactions is correct is that only in the northern part of the U S.A can it be inferred that almost all the children around 10 years of age who have reactions of 6 mm. or more to 5 T U are infected with tubercle bacilli In southern India the proportion falls to 50%, and in England it is roughly 85%

As we have previously said [2] the description 'non specific used by the W H O workers for this type of sensitivity is misleading It implies that the reaction is due not to sensitivity produced by infection with a *particular organism but to a general change in the* sensitivity of the skin to many stimuli Moreover it implies that the tuberculin reaction to human type purified protein derivative is specific for human type tuberculous infection This is not true as the W.H O teams have themselves demonstrated The mean size of the reaction to 10 T U in adults in Denmark was found to be related to the past prevalence of tuberculosis in cattle, a greater mean size being found in districts with a previously high prevalence and, therefore in populations subjected to greater risk of bovine infection [3] Cattle infected with mycobacteria other than *Mycobacterium tuberculosis bovis* become sensitive not only to tuberculins prepared from the infecting mycobacteria but also to bovine tuberculin. But the homologous tuberculin

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1. Mayer-Gross, W Slater E. Roth M Clinical Psychiatry London 1954
2. Overholser W The Psychiatrist and the Law New York 1953.
3. Carroll, R. E. Sinton W Garcia A *J Amer med. Ass.* 1955 157 422

1 *Bull Wld Hlth Org* 1955 12 63.
2. *Lancet*, 1954, i, 241
3 *Bull Wld Hlth Org* 1955 12 2 7

usually causes a larger reaction than the heterologous tuberculin[4] The W H O investigators tested many people in India with equal quantities of both human and avian tuberculin[5] Those showing a high degree of sensitivity to human tuberculin, presumed to be infected with human tubercle bacilli, gave smaller reactions to the avian tuberculin But in the group reacting only to large doses of human tuberculin the reactions to avian tuberculin were the larger It is not suggested at present that the low-grade sensitivity is caused by infection with avian tubercle bacilli, although disease in man can indeed be caused by these organisms[6 7] The cause of the sensitivity may, however, be more closely related to avian than to human *M tuberculosis* There are many other mycobacteria in man's environment, and the observed low grade sensitivity may be due to infection by several of these at once, the particular agents varying in different localities But the sensitivity is neither more nor less specific to a particular mycobacterium than is the sensitivity produced by human tuberculosis It seems preferable to call these reactions to small doses of human tuberculin "non-tuberculous" It might, of course, be objected that infection by any type of *M tuberculosis*, including avian bacilli, is a tuberculous infection, but the proposed term certainly has a greater practical value, for it implies that the reactions do not have the same diagnostic and epidemiological significance as the true "tuberculous" tuberculin reactions

## HANDWRITING AND THE PSYCHE

READING the character from the handwriting used to be an elegant parlour game, at which a few intuitive people managed to excel That handwriting may provide clues for psychiatric diagnosis is a more recent idea Captain William R Perl,[8] chief clinical psychologist at the United States Disciplinary Barracks at Fort Leavenworth, Kansas, says that it is based on the assumption "that an individual is self-consistent, and that such self consistency is reflected in one way or the other by *all* his behaviour and actions" He adds two facts which he holds to have been established experimentally (1) that handwriting is both a product and a permanent record of a person's highly individual motions, and (2) that "there is an intricate and interpretable relationship" between a person's motions and his emotions We write (most of us) with some regard for legibility, under the influence of contemporary style, and within an arbitrary alphabet, but these limitations apart, we show a luxuriant variety in the use of the pen It is not the hand that writes, however—it is the whole man People who lose their hands and learn to write holding the pen in the mouth or between the toes go on forming the letters in their accustomed way Two specimens of Nelson's handwriting, reproduced in Perl's article, show that his letters sloped forwards while he was still using his right hand, and on the whole backwards when he was obliged to use his left, but they are essentially the same letters the word "Battle," which occurs in both samples, has the same capital "B," made like a "13," the same interruption after the initial, the same long first "t" and smaller second "t," and the same sort of cross-bar Captain Perl does not note, as he might have done, that during the ten years separating the two samples Nelson had acquired a Greek "ε"—an affectation which, in adolescents, sometimes signifies an ungratified wish for importance It would be interesting to know what it signified in one who was already a national hero

The individual character of handwriting starts early—from the first writing lesson, in fact All the children in a class may learn together from the same teacher, and using the same fixed copy, but, Perl says, "one child will use up the writing space with a few bold strokes, while another, expressing his personality, will hide his weakish and wavy lines in one corner of the space One writes with meticulous care, thus displaying compulsive elements, while the other will not care for the details, solve the problems carelessly, with untidy result" Pressure in handwriting probably tells something about the psychological state of the writer, though it must not be considered, Perl suggests, in isolation, but only as part of a constellation Strong pressure, often interpreted as a sign of energy, may in fact indicate neurotic tension, it may also (though he does not say so here) indicate a mood of anger, or of enthusiasm He describes pressure as "the graphic record of our reaction to the resistance created by the friction between paper and pen", and the way in which we overcome this obstacle of friction may possibly indicate something about our general method of dealing with obstacles The writer who overcomes the friction by driving his pen forcefully is not necessarily a forceful person he may be confused and disorganised by the problem—weak, in fact, rather than strong The man who, instead, moves his pen lightly to reduce the friction may not be weak he may be one who does not waste energy needlessly but who adapts himself to his opportunities

Something of the character of the writer inevitably appears in his signature, and in the letter "I" The self-confident "I" of the man who invites inspection is very different from the mild and unassuming "I" of the meeker man The signature, often expansive and dashing in early youth, settles in time into the form which the owner wishes to present to the world large or small, simple or showy, precise or vague But it is not, even then, beyond change make a man a dictator and his signature suffers accordingly Reproductions of Mussolini's signature from the time when he was a fairly unknown journalist, and wrote a modest schoolboy hand, to the time when he was a fully fledged dictator show the deplorable inflation of his self regard

Physiologically, handwriting is the result of muscular contraction and release, the balance between them giving rhythm, and study of this rhythm in patients who are mentally sick may prove useful, Perl suggests, in psychiatric investigation Disturbances of rhythm are not seen in cyclothymic patients The manic patient's handwriting, though often large and exaggerated, has a smooth, flowing, and even accentuated rhythm, and the writing of the depressed patient, though it may sink gloomily downwards from the start of the line, and though the letters may be blunted and toppling, yet flows rhythmically across the page The hand of the schizophrenic, however, shows a broken rhythm, suggesting a loss of balance between muscular contraction and release Perl suggests that a casual inspection of a patient's handwriting may sometimes be enough to set his doctor on the right diagnostic track, or lead him to counsel psychiatric investigation The method, when it is more fully developed, may also, he thinks, throw light on the psychology of those historical persons who have rashly left us specimens of their handwriting

## F R S

AMONG the twenty-five new fellows of the Royal Society we are glad to see the names of three members of the medical profession—namely, Prof A W Downie, of Liverpool, Prof K J Franklin, of St Bartholomew's Hospital, and Sir Harold Himsworth, of University College Hospital and the Medical Research Council

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SIR GODFREY HUGGINS, on whom a viscounty has been conferred, has chosen the title of Viscount Malvern of Rhodesia and of Bexley in the county of Kent.

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[4] Green H H *Vet J* 1946 102, 267
[5] *Bull Wld Hlth Org* 1955, 12, 85
[6] Bradbury, F C S, Young, J A *Lancet*, 1946, i, 89
[7] Dragsted, I *Ibid*, 1949, ii, 103
[8] *Amer J. Psychiat* 1955, 111, 595

## Special Articles

# METALLIC POISONS AND THE NERVOUS SYSTEM*

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IN clinical neurology the metal which has provoked most interest lately is copper, which in hepatolenticular degeneration is excreted in the urine and deposited in excessive quantities in the liver and basal ganglia umings 1948) Nevertheless occupational poisoning with copper seems very uncommon (Heyroth 1949) and neurological involvement has not been recorded Industrial poisoning with manganese produces a clinical picture remarkably similar to hepatolenticular degeneration

### MANGANESE

The first account of manganese intoxication was given in 1837 by Couper who described its effects in 2 men employed in grinding manganese peroxide in the manufacture of bleaching powder Little further interest was taken in the condition till the 1920s Charles (1927) described 11 cases in England and a number have been reported from other countries (Edsall et al 1910 Flinn et al. 1941 McNally 1935) including 75 from Chile Jiminez et al 1946) Most patients have been men employed in mining and separating manganese ore

*Clinical Picture*

The neurological involvement is insidious in onset and slowly progressive as long as the patient remains exposed to manganese dust There is fatigue on exertion rigidity of the limbs and trunk, and a tendency to walk on the metatarsal joints the patient's face becomes expressionless (with at times a spastic smile) and he displays emotional lability—smiling and laughing hilariously without adequate cause—and a coarse tremor of the head and limbs, sometimes of intention type From the clinical descriptions and photographs given in Charles's paper the condition resembles hepatolenticular degeneration and some forms of postencephalitic parkinsonism rather than degenerative paralysis agitans There is no mention in the various papers of a corneal ring comparable to the Kayser Fleischer ring but it is not clear how thoroughly the corneas have been examined

*Pathology*

A detailed post-mortem examination of the brain of a man who died of cardio renal disease fourteen years after exposure to manganese and who had characteristic neurological symptoms was made by Canavan et al in 1934 There were diffuse cellular changes in the cerebral cortex and cerebellum but the significant changes were in the basal ganglia with little difference in intensity between the caudate nucleus the putamen the globus pallidus and the thalamus. Similar but less detailed findings have been recorded in other cases and cirrhosis of the liver has also been found in patients with chronic manganism In monkeys repeated intraperitoneal injections of manganese chloride have produced gross pathological changes in the liver and lenticular nucleus (Mella 1924) and in rabbits dogs and rats chronic manganese poisoning has caused diffuse cerebral lesions with maximum incidence in the corpus striatum (Tolyskoya 1952) There is a close clinical and pathological similarity between chronic manganism and hepatolenticular degeneration but the cause of the specific affinity of manganese and copper for the basal ganglia and liver remains undiscovered

### MERCURY

The dangers of mercury have been recognised since the time of Pliny (Hunter 1935) The two predominant neurological symptoms are erethism and tremor

*Erethism* is the name given to the curious psychological state which is often the first symptom sometimes in association with stomatitis The sufferer becomes unusually tired is easily upset and embarrassed, is in constant fear of losing his job dislikes meeting people and easily loses his self-control The word has been said to be derived from ἐρυθρός, red to describe blushing embarrassment of the sufferer" (Buckell et al 1946) but the Oxford English Dictionary derivation which would seem the more probable, is from ἐρεθίζειν to irritate.

*Tremor* is usually a later symptom affecting the hands (making writing difficult) the face the tongue, and the legs The tremor is considerably coarser than in thyrotoxicosis and the combination of tremor difficulty in articulation and mental symptoms may confuse the diagnosis Some years ago I saw a patient who had been admitted to hospital with the provisional diagnosis of general paralysis of the insane and the correct diagnosis of chronic mercurialism became apparent only when it was realised that his work consisted in filling thermometers with mercury

Mercurialism has occurred in a number of occupations the best known of which is probably the felt-hat industry There mercury nitrate is used in the carrotting process, in which the smooth resilient hairs are made rough and limp to facilitate felting This danger gave rise to the phrase as mad as a hatter' which *Alice in Wonderland* later made familiar

Recently attention has been drawn to mercurialism arising in an unusual way

> In criminal investigation grey powder is often used to bring out finger prints because it has a special affinity for the sweat formed latent prints and produces a good print for photographing A body of men specially trained in this work is employed in the Lancashire Constabulary and investigation of 32 of these men in 1949 by Agate and Buckell disclosed 7 with mercurial tremor 1 being severely affected in 4 there was evidence of erethism either at the time of examination or in the past history As a result of this a powder not containing mercury has been substituted for grey powder in that particular police force Some years earlier in Denmark lead poisoning was diagnosed in a policeman who had been using white lead to develop latent finger prints (Nyfeldt 1937)

In 1951 chronic mercurialism was recognised in 5 men employed in repairing direct-current electric meters (Bidstrup et al. 1951) The first of these 5 cases is of special interest

> He developed tremor of the hands arms, and legs together with irritability and stammering and disseminated sclerosis was diagnosed Some time later when his condition had deteriorated he read a newspaper account of mercury poisoning in the Lancashire policemen just referred to He told his doctor that his work involved handling mercury and in this way the diagnosis was eventually reached 4 other men doing the same work were also found to be affected

Direct current meters contain a mercury bath in which an armature revolves between the poles of a magnet The armature disc becomes coated with a rough amalgam which has to be scraped off as it turns in a lathe, and during this stage of cleaning small particles of mercury may be carried into the atmosphere this was thought to be the cause of the mercury poisoning

Mercury in teething powders has been suggested as a cause of pink disease in infants (Warkany and Hubbard 1948 Farquhar 1953 Dathan 1954) and high urinary levels of mercury have been found in this condition

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* Based on a paper read to the section of neurology at the annual meeting of the British Medical Association in Glasgow July 1954

### METHYL MERCURY COMPOUNDS

An entirely different neurological picture from ordinary mercurialism is seen in poisoning with methyl mercury compounds. The first 2 cases (Edwards 1865, 1866) were in 2 laboratory workers at St. Bartholomew's Hospital who were using dimethyl mercury in research on the valency of metals. These 2 men developed numbness of the hands, ataxia, impaired vision, and mental dullness progressing to confusion, coma, and death, while a 3rd man affected similarly but less severely made a very slow recovery. In 1940 Hunter and his colleagues investigated 4 men who were poisoned by the inhalation of methyl mercury compounds in a factory where fungicidal dusts were manufactured without the use of completely enclosed apparatus. These men developed ataxia, dysarthria, and gross constriction of the visual fields without changes in the optic discs or retinæ.

*Pathology*

In 1954 Hunter and Russell reported the post-mortem findings in 1 of these patients who had died of heart-failure. The important changes were severe atrophy of the medial surface of both occipital lobes, particularly about the anterior end of the calcarine fissures, and gross atrophy of the folia in the depths of the sulci in both lateral lobes of the cerebellum, posterior to the primary sulcus. Microscopy showed severe loss of neurones in the atrophic areas of the occipital lobes, while in the affected areas of the cerebellum there was profound loss of cells in the granule cell layer with general preservation of Purkinje cells. No abnormality was found in the spinal cord or nerve-roots. This curious selective atrophy in the occipital lobes and cerebellum probably accounted for the gross constriction of the visual fields and the general ataxia.

### LEAD

Because of preventive measures, industrial lead poisoning of any severity is very rare in Britain; but it is still occasionally found outside industry. Three years ago twin girls, aged 2, were admitted to St. Bartholomew's Hospital with plumbism (Millichap et al. 1952). 1 had anæmia, slight jaundice, and peripheral neuropathy affecting the anterior tibial muscles, and the other only anæmia; both had punctate basophilism, "lead lines" in the long bones, and a high blood-lead content. It was discovered that their cots had been painted with lead paint by their father and the children had regularly gnawed the newly painted cots. Other similar cases have been described, and also acute lead encephalopathy in breast-fed infants whose mothers were using lead nipple-shields (Burrows et al. 1951, Gordon and Whitehead 1949). Recently the homely "iced lolly" has been suggested as a potential cause of lead poisoning (Semple 1953), though no actual case has been described. Iced lollies may contain up to 11 parts per 1,000,000 of lead together with copper, zinc, and tin which are absorbed from the metal moulds in which the water and coloured syrups are frozen.

The neurological symptoms of lead poisoning are well known, but two aspects are worth some discussion—the nature of the so called neuritis, and the recent suggestions for using a chelate in treatment.

*Lead neuritis* is unlike any other type of peripheral neuritis in that it is purely motor (usually involving only limited groups of muscles), is not restricted to individual peripheral nerves or roots, and may involve either proximal or distal parts of the limbs. As a rule the muscles involved are those which the patient uses most constantly. Though the commonest form involves extensors of the fingers and wrist with sparing of abductor pollicis longus and brachioradialis, it may affect the shoulder-muscles of men whose work involves much lifting, the legs of potters who turn their wheels by foot pressure, and the finger and thumb muscles of the left hand of file-makers who grasp a chisel firmly in this hand in the process of file cutting (Cantarow and Trumper 1944).

These observations suggest that the effect of lead may be primarily on the muscles rather than on the peripheral nerves or nerve roots, and experimental evidence favours this view.

Reznikoff and Aub (1927) showed that the diffusion of inorganic phosphate from isolated muscles is greatly increased after exposure to lead, and that such muscles fatigue more rapidly than normal. In 1930 Lundsgaard established that the energy for muscle contraction is provided by the break-down of phosphocreatine into creatine and inorganic phosphate, both of which can diffuse freely through the muscle membrane. Steiman (1939) found that in the muscles of animals exposed to lead the resting level of phosphocreatine was much reduced, and that after a two minute tetanus there was practically no resynthesis of phosphocreatine, whereas normally complete resynthesis took place within half an hour. The force of muscle contraction is recognised to be proportional to the breakdown of phosphocreatine, and these experimental observations strongly suggest that the cause of the muscle weakness in lead palsy is a disturbance of resynthesis of phosphocreatine in the muscles—possibly by the action of lead on intracellular enzyme systems—rather than a neuropathy.

The accepted *treatment* of lead poisoning in the more acute stages has been to encourage the deposition of lead in the skeleton by means of a high-calcium diet and the administration of calcium, together with symptomatic measures such as the reduction of raised intracranial pressure in encephalopathy and physiotherapy in lead palsy. When symptoms subside it is sometimes difficult to decide whether to attempt to mobilise the lead from the skeleton by giving a low-calcium diet along with ammonium chloride or potassium iodide, or whether to leave the lead deposited in the skeleton. Mobilisation of lead in this way sometimes results in exacerbation of toxic symptoms, while if the lead is left in the bones symptoms may arise later during an acute infection or after an operation. Dimercaprol (B.A.L.) has been used, apparently with success, in some cases (Bastrup-Madsen 1950), but, although the excretion of lead in the urine may be increased considerably, there is a real danger of an increase of the symptoms from the redistribution of lead in the body tissues (Vigliani and Zurlo 1951).

Recently a new approach to the treatment of lead poisoning has been suggested, involving the use of a chelate (Foreman 1953). A chelate is a type of chemical compound which does not ionise. Ethylenediamine-acetic acid (E.D.T.A.) forms chelates with certain metals, in particular calcium and lead, which are water soluble and non-toxic and are excreted in the urine unchanged. Fortunately the affinity of this substance for lead is considerably greater than for calcium. The rationale of the treatment is that after administration of calcium E.D.T.A., calcium will replace lead in the body and lead E.D.T.A. will be carried in the blood-stream and excreted in the urine; because the chelate does not ionise there will be no danger of exacerbating the symptoms of lead poisoning.

In laboratory animals calcium E.D.T.A. has been found to remove lead and certain other heavy metals such as yttrium, americium, and plutonium. The number of patients treated is still small, but in the United States Rubin (1953) reported moderate clinical improvement in a child with acute plumbism, and Foreman and his colleagues (1953) mention 5 children and 3 adults in whom pronounced alleviation of symptoms and a considerable increase in lead excretion followed treatment with calcium E.D.T.A.; there was no evidence of toxic side effects, and there were no symptoms attributable to mobilisation of lead. In England Giles et al. (1955) have reported successful treatment of a child, aged $2^{1}/_{2}$, with acute lead poisoning. These preliminary results suggest that calcium E.D.T.A. chelate may have an important place in the treatment of lead poisoning.

*References at foot of next column*

# LESSONS IN WARD 10

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N F U

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AT a casual glance these children with bronchiectasis seem to have the exuberance of a normal child but on closer inspection most of them appear to be thick with a perpetual cold, and to have the listlessness of a general septic condition. Here is material to challenge the ingenuity of the teacher, who has to conduct school in the midst of a highly organised hospital life with children eager, yet of limited capacity.

The world of these children has been narrowed by their disability. Apprehension on the part of the parents has, perhaps, led to over protection and consequent frustration of the child. Attendance at school has been irregular, resulting in backwardness and lack of self confidence. Moreover a child who seems to have all the symptoms of a chronic cold has little chance to develop latent abilities in the social activities of a school.

When the child first enters a hospital ward and finds that the routine of schooling is expected of him as usual, even in this strange world he may well look upon the teacher as his one link with a normal life. The initial impact of hospital life can be alarming. Derek said "When I first went into Ward 10 I was frightened because I did not know anyone. It also worried me very much to see the surgeon walking about with his operation uniform on." The children have to adjust themselves to a world of strange faces unusual equipment, and many investigations. Instead of the atmosphere of the normal classroom school takes place in the open ward where nursing routine must go on. Treatment must come first, medical staff must do their rounds and X rays must be taken. With all these claims on the child's time the school could not run smoothly enough to have real value unless all departments coöperated generously in keeping school hours (9.30–11 30 and 1 30–3 30) as free from interruption as possible.

In this ward of twenty beds most of the children are up all day unless they have had an operation. The length of stay may be anything from three weeks to six months. Children aged from 2 to 12 are on the school register, and this gives an average class of fifteen for even bed patients are anxious to attend.

### Active Learning

The activity method has been found the most successful way of teaching these children. Its essence is to concentrate on a centre of interest common to the group, and in the development of such a project a wide range of time table subjects will be covered. Children come and go but some activity will present itself which can be completed at short notice if the interest wanes the children flag or some of the group are discharged. A wide age range can work together and the method gives a creative rather than destructive outlet to pent up energies of children confined to hospital routine.

Fig. 1—With gloves on John overcame the fear of the pet grass-snake.

Joining in activities designed to suit their own condition the children are not put at a disadvantage by their disability. They gain confidence because each can contribute something to the group. They can work at their own pace and relieved of the competitive pressure of a large mixed class, may well make up for the schooling they have missed. They become more self reliant as they develop a feeling of achievement and pride. Moreover much of the work leads them to explore the resources of the town and country on their doorstep and so make valuable new educational and social contacts. With a small group one can carry out projects impossible in schools. Also, the great interest shown by hospital staff and the local community has provided a wide background for these activities.

For these children a rigid time table is not only impossible but harmful because the scheme for the day must meet the special needs of the group at that moment. A well planned time table of the night before may have to be abandoned. A death, an operation new staff or patients, or disturbances since getting up at 5 30 A.M. may have unsettled the whole ward.

### Some Activities

One most rewarding venture is the yearly pantomime at Christmas in which every child from the age of 3 takes part. The plays for instance *Cinderella* and *The Sleeping Beauty* written by the children as a group, take the form of a traditional pantomime including dancing

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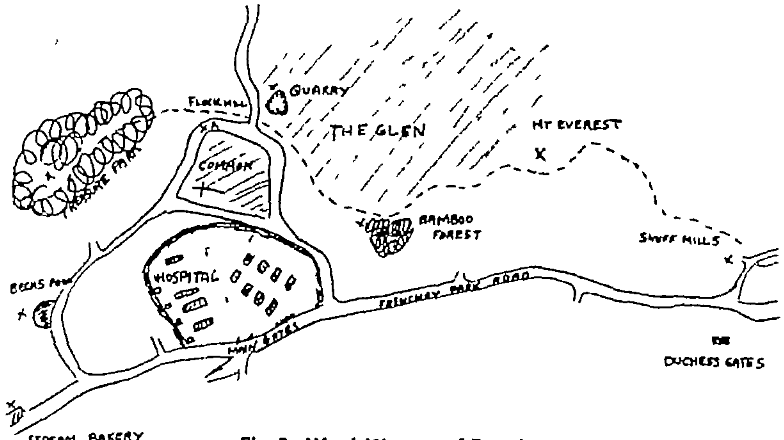

Fig 2—Ward 10's map of Frenchay

singing, and of course a theme song There has been great competition to produce the neatest programme and invitation and the most striking poster The children are allowed to use the hospital stage Producer, property-man, and stage hands are chosen from the group, and on the great day they are in control of the show Of the 14 performers last year, not one had acted in a play before, put on make-up, or used a proper stage

The pantomime is an example of an activity that needs an audience Besides the creative work which goes into entertaining it, the organisation of the party involves writing and arithmetic On an open day, such as this, the children find themselves hosts as the world walks in Aware of the responsibilities they have incurred, the group rises to the occasion, carrying off what is to many of them a new situation with an assurance which surprises themselves and adds to their stature

We have also invited audiences to exhibitions

The pottery exhibition came into being after a visit to one at the museum Luckily, it coincided with clay modelling in handwork Because of discharges the scheme had to be completed within a fortnight A short history of the craft was given and the children chose and mounted pictures to show the development of the craft Posters gave particulars of the event, which was open to the public for a week, and some of the children's work was shown Visitors were invited to "try to make something" at a table prepared for them. Pottery was lent by well wishers and samples of craft processes by a local pottery Notices printed by the children, and a small library of suitable books, were also on view

Finally, the children were taken to a brickworks some distance away and came back armed with enormous lumps of clay—of a type very suitable for experiments Peculiar objects were made, fired by the brickworks, and taken home as evidence of achievement by proud owners

An art exhibition followed closely on the heels of the opening of the Royal Academy one season

Children's paintings had been kept throughout the year, and a children's committee selected fifty to be hung These were numbered and catalogues printed Their posters advertised the coming event, which was to be officially opened by the surgeon of the unit The committee prepared the room, polished the floor, arranged the flowers, and helped with the hanging They joined in the agonising experience of the ones chosen to address the assembly, introduce the speaker, and call afterwards for a vote of thanks, in the best Royal Academic manner

Heralded by exciting posters, summer was once marked by a fete, complete with barrel organ and monkey, and hand made goods for sale on the stalls

There is always a pets' corner in the ward, and the care and observation of its occupants is of great value to these children The vivarium is exciting and there are frequent pond dipping expeditions to restock the aquarium Staff have been tolerant of grass snakes in trouser pockets and hamsters nibbling biscuits on a bed patient's locker The library and Nature table are other permanent features in the ward, a centre of interest to newcomers who think they are going to be put to bed and stay there, and a comfort to returning patients

A visit to the Zoo is a delight to both children and escorts, the keepers allowing the party to go behind the scenes After one such visit a child remarked, "Why don't we have a Pet Show ?" The bomb exploded, the show was on—a never-to-be forgotten experience! Besides more normal animals, exotically beautiful birds and fish (many prizewinners at fanciers' shows) graced the end of the ward , and the grand finale was the arrival of a lorry-load of animals lent by the Zoo, including monkeys and two laughing parrots The show aroused great interest among adults as well as children and softened many a heart Others were only too willing to discuss their hobby or particular pet, and after two hours it had to be closed, and the visitors forcibly ejected

Two activities, more literary in character, took the children out into the local communities in search of material On one occasion a booklet about the village was compiled, written, and printed A group of children aged 10–13 worked on their own Local firms were approached, and a mill, bakery, and quarry were visited The group paid these visits alone, with the responsibility of maintaining the social courtesies Records were made of what they had seen and letters of thanks sent

The children also decided to write about the walks they knew for the benefit of weekend visitors, and this led to lessons on elementary map work, and a plan of

Fig 3—Gathering berries for the harvest festival

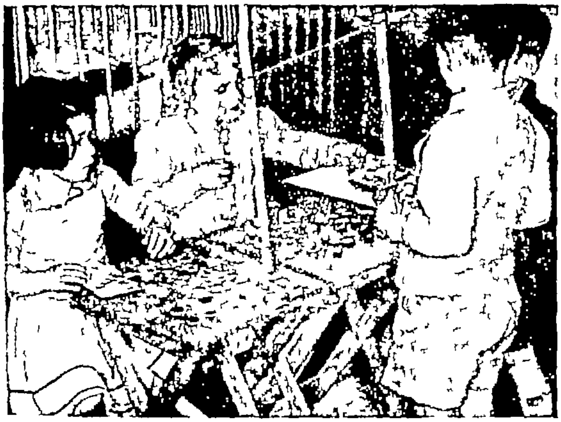

Fig 4—A busy morning at the bank.

the hospital and village was made From these two projects the idea of the guide book was born Part I describes local industries and part II interesting walks with a short description of the church and stories about the village. Again the children found themselves note book in hand in new social contacts with local people Finally, the children saw their book being printed on a duplicating machine and were responsible for selling 125 copies and balancing the accounts

One term we had a weekly ward newspaper

> All news was given verbally or in writing to a member of the committee Every Monday morning at the conference headed by the editor an 11 year-old girl, the copy was arranged and blocked for printing Four children working as a team were able to cyclostyle 30–40 copies in an hour and these were sold next day For the older children ward news was extended to include a world news scrapbook and a visit to a newspaper office

Whenever possible tradition is upheld and festivals celebrated, linking the children with life outside the ward Every Christmas the children make a crib, also cards wrapping paper and presents They decorate a tree hold a party, and give hand made presents to their parents, and end with carol singing Autumn was marked by a Harvest Festival and Halloween and Nov 5 are eagerly awaited

These are special festival times with their own magic to offer the child but they may not perhaps cover the three R s Here are some examples of popular activities which do

> A general store is a favourite with all ages and develops according to the group A bank and a bus are usually added Once a post office appeared and the children visited a nearby post and sorting office Back at school they learned how to telephone and send telegrams—all pocket money was spent that week. They enjoyed lessons on the history of the Royal Mail and began to collect stamps
>
> Another time a village grew round Mrs. Muggins Stores. Each child became a character in the village and Dr Jones Mr George of Dragon Farm and Miss Smith the school teacher did far more letter writing and work than John, Henry and Mary A large picture map of the village was painted and houses, farms, fields, and woods were named The village magazine reported such things as a burglary at the Manor an accident at the crossroads, a fire and trouble on Badger s Common with a gipsy encampment not to mention hate letters from Mrs Muggins to Miss Smith about her badly behaved children. This project owed a lot to a child who was very active both mentally and physically but was confined to bed.

### School Report

The activity method does not take up all the school time The children enjoy routine work for part of the day or at some time during the week. A weekly record is kept, and time table subjects omitted or not covered by an activity are inserted to secure a balanced weekly diet of work.

But the physical, and sometimes mental, state of these sick children often makes it impossible for them to concentrate on school work without an absorbing centre of interest to take their minds off their illness This the activity method provides It also allows them to go at their own pace and gives the teacher the necessary flexibility in arranging a time table to suit changing ward conditions and a shifting population

The children stay for such short periods that it is hard to assess their progress in each traditional time table subject It is even more difficult to assess the eventual educational benefits which they receive from their visits, contacts and researches in the world outside and the activities they organise But the development of character which this method encourages is more visible Responsibility and a sense of achievement seem to give more confidence to the shyest child The children who come to the ward school seem more lively and alert than those who have individual lessons on adult wards

The therapeutic value of school is obvious The anxiety of children to be allowed to come back to school after an operation may shorten their convalescence Often a child too ill to do lessons has pleaded to be wheeled up in bed to the class Then satisfied, he falls asleep

I wish to thank Mr R H. R Belsey surgeon in charge of the unit for his interest and support.

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# Public Health

## FRENCH PUBLIC-HEALTH SERVICES

J S Cookson
M.A. M.D Camb., D.P H

COUNTY MEDICAL OFFICER HEREFORDSHIRE

Last year I spent two months in France studying the French public health services First I spent six weeks in the department of the Aisne where I watched at close hand the working of the ordinary public health services and the other medical and social services of a rural county particularly the public health centre at Soissons My last two weeks I spent in Paris studying the administrative arrangements of the French ministry of health

The central authority in France is the ministry of health and the minister is responsible for the public health services to the elected legislative assembly Outside Paris, the department is responsible for providing the main public health services These services are financed partly by the central government and partly by the department and the commune The department is advised by the *medecin directeur départemental de la santé* His terms of appointment are interesting Though he serves the department he is appointed by the ministry and is an official of the central government His duties range from purely advisory functions so far as hospitals and sanatoria are concerned to those of an executive nature for public health

### PRENATAL AND POSTNATAL SERVICES

By and large, the public health services in the department of the Aisne are comparable with those of an

English medium-sized rural county, but there are differences.

In France a premarital examination is compulsory. The engaged couple must have a full clinical examination by their local doctors, supplemented by special examinations to detect tuberculosis and syphilis, the diseases most likely to be transmitted to spouse, or to possible children. If the medical examination is unsatisfactory this is not a bar to marriage, but it gives the doctor an opportunity of explaining the dangers. The certificate does not give any diagnosis, but merely states that an examination has been made. It must be delivered to the official at the registry office. It is difficult to know how useful this procedure is, but it does something to make engaged couples aware of their responsibilities to each other and to future generations.

When the birth of a child is registered, the proud parent is presented by the Mayor with a *carnet de santé*, which is a booklet in which the *assistantes sociales* record physiological or pathological particulars as the child develops. It serves as a useful reminder to a mother with a large family to see that each child has been vaccinated or inoculated against infectious diseases and, not least important, that she has made the proper claims to the *caisses* (government friendly societies), for benefits.

Vaccination against smallpox is compulsory and it is supposed to be carried out during the first year of life. Combined inoculation against diphtheria and tetanus is also compulsory between the ages of 12–18 months. In practice, doubtlessly a number of children do not receive these prophylactics at such an early age, but there is a useful check when the child goes to school, since he will not be accepted unless he has been vaccinated against smallpox and immunised against diphtheria.

### SCHOOL HEALTH SERVICES

This service is under the department, but it is completely separate from the other health services. The compulsory school-age is 6–14 years; actually many children of 4 and 5 years of age attend and there seems to be adequate accommodation for them. There is no school on Thursdays, but all day on Saturdays. This mid week break is appreciated by children and staff alike.

All children are medically examined every year at school. The examinations are made at great speed, 30 per hour, giving a total of up to 120 a day. An *assistante sociale* visits the school the day before, weighs, measures, and examines the child for personal cleanliness. The medical officer with whom I worked insisted on each child being stripped, which is by no means the universal practice in England.

Many children came from poor homes, but I saw few flea bites or verminous heads.

The medical officer was helped by two *assistantes sociales*. One completed the medical cards and the other wrote a letter to the parents of each child, even if all was well. If necessary a personal letter was also sent for the parent to take to the family doctor.

It is compulsory for all teachers to be medically examined on entering the profession. I watched teachers having their annual X-ray chest examinations by the tuberculosis officer. Much importance is attached to these examinations.

Where children are living in overcrowded conditions, particularly in the larger towns, arrangements are made for them to spend the summer holidays in *colonies de vacances*. These are for children between the ages of 6–14 years. The colonies are in large country houses, which may be used for other purposes outside the holiday season. There are also *colonies sanitaires*, which are open all the year round for debilitated and convalescent children of all ages. Their aim is prevention rather than cure.

I found an excellent *centre de l'orientation professionelle* at Soissons run by a psychologist. His main job was to place school-leavers at 14 years of age. He interviewed only those children whose parents wanted his advice. He examined the children by standard intelligence and vocational tests. Later he asked the parents to come with the child for a discussion. He put the parents in touch with training centres for boys, usually at Lille, and for girls at Rheims. He explained to me that in France most girls wish to become good wives and mothers, so they prefer good domestic training.

### SOCIAL WORKERS

In England we are trying to define the kind of health and welfare worker best qualified to meet the needs of the family efficiently yet with the greatest economy of time, money, and woman power. Our problem is to have home visits made by a social worker experienced in a particular branch of social work and yet avoid a multiplicity of visits by specialised social workers. The experience of France with *assistantes sociales* merits serious attention.

The training, final examinations, and registrations of the *assistantes sociales* are under the direct control of the ministry of health, even where the training is given in schools which are not their direct responsibility. Girls who take up this work are advised first to take their full nurses' training course, which in France lasts only two years. After this training they have an eighteen month course rather similar to our own health-visiting course. The theoretical part of the curriculum is standardised for all students, but each student is allowed to choose which type of practical work she wishes to do. She is thus able to specialise at an early stage in the branch of social work which she intends to do after qualification. The tutors encourage students to undertake work for which they are likely to have some aptitude.

On the face of it, this form of training seems to work out well in France. It would be less suitable for England because the *assistantes sociales* are not trained in midwifery, and the coordination of the domiciliary midwifery and district nursing in rural England has much to commend it.

### AN EXPERIMENT IN PUBLIC HEALTH RESEARCH

In 1949, as part of the programme of post-war reconstruction, it was decided to set up in the region of Soissons, with a population of 150,000, an experimental centre of public health. It was felt that the first step must be to improve, extend, and coördinate the existing services so that this part of rural France would be not only up to normal standard but even something of a show place. The hope was that, when this had been achieved, the centre could be used for educational purposes.

The centre is now open, and Dr. Lataillade, the medical director, has wisely established his offices within the curtilage of the Soissons Hospital. The centre is superimposed on the existing public health organisations and receives considerable financial support from the Rockefeller Foundation, the World Health Organisation, and the International Children's Fund. Its functions are varied and, so far as France is concerned, experimental. At the time of my visit they included the following:

Regular monthly talks on topical medical matters. I had the privilege of hearing one given by Professor Thieffry, of the Faculty of Paris, on poliomyelitis. These talks are well attended and are common meeting ground for doctors in all branches of the profession within reasonable access of Soissons.

A pædiatrician from Paris visits the centre each week mainly to see cases referred to him from the well baby clinics."

Surveys are made on special public health problems At the present details about all physically handicapped persons in the department of the Aisne are being collected In view of the special problems of France this is not so easy as it would at first appear

A mass miniature-radiographic survey was being made of the hospital staffs in Soissons and the surrounding villages where it was thought that there was an undue prevalence of pulmonary tuberculosis. The apparatus had been presented by UNICEF

Regular statistical analyses are made of vital statistics A statistician comes from Paris to advise on this work and to guide research into useful channels.

A child guidance centre has been set up staffed by two psychiatric social workers a part time visiting educational psychologist and a psychiatrist This service is in its infancy in France

There are obvious difficulties in grafting a public health centre on to existing public health services But there are advantages in having a centre properly staffed with trained workers who have time for original research without being unduly concerned with routine administration Perhaps in the future the centre will be useful as a postgraduate institute where French and foreign workers particularly from underdeveloped countries will study rural public health administration

### GENERAL PRACTICE

French general practitioners all seem to be strong individualists sensitive to and much against, any interference from the State There is a powerful professional body, known as the Syndicate, which deals with professional matters and which is held in respect by all doctors There is also a committee which is an official body and is said to deal with disciplinary matters.

A usual charge in the country for a consultation at the surgery is about 8s, and for a visit about 12s, depending on the mileage The patient pays the doctors and then recovers from one of the government friendly societies—the *Caisse de Société Général* in the town, or the *Caisse de Mutuelle Agricole* in the country If the patient is unable to pay, the doctor gives him free medical care and himself recovers the fee from *Assistance Médicale Gratuite* which is something like our old parish relief

A high proportion of pharmacists have been trained in laboratory investigations Behind the ordinary chemist's shop it is usual to have one side devoted to dispensing and the other to laboratory work This service is extremely popular with the local doctors who often need simple laboratory investigations but have not the time to undertake them All pharmacists are registered by the department and a control is kept on their prescriptions by occasional reference for analyses to Paris The patient pays the chemist when he collects his medicine and recovers a proportion (not exceeding 80%) from the government friendly societies. If the patient is unable to pay the chemist supplies him with the medicine and himself recovers the fee from the *Assistance Médicale Gratuite*

Spectacles are usually prescribed by an ophthalmic practitioner and made up by an optician He orders them from a factory but takes an interest in selling the most suitable frames to the patient The government friendly societies contribute up to a quarter of the cost for approved lenses and frames.

### INDUSTRIAL SERVICE

The industrial medical service is well developed and all factories both public and private, must have adequate medical and ancillary services. In Soissons with a factory population of 5000 there were two whole time factory doctors All young people aged 18 years were medically examined before beginning factory work, and all workers were examined annually They came, so far as possible, to the industrial medical centre, which was reasonably well-equipped with a laboratory and an X ray unit The two doctors also visited regularly all factories to inspect industrial hazards Each large factory had one or two trained nurses Where home visits are required for welfare purposes these are made by the *assistantes sociales* of the department

### CONCLUSIONS

The French medical services are different from ours and perhaps we have something to learn from them, though what is suitable for France is not necessarily ideal for England

Their school health services are not so well developed as ours.

The work of the *assistantes sociales* is important. It is preferable to have only one social worker visiting the home if she can call on specialist advice.

The public health research centre at Soissons is an interesting experiment for it has money, trained workers, and time to spend on research

I am indebted to the Ciba Foundation and the National Institut d'Hygiène of France, for grants which made my visit possible

## The Rôle of Local-authority Clinics

A good deal of thought continues to be given to the future of local-authority clinics and the place they should occupy in the health service Quite apart from the discussions on how these centres may play a part in the prevention of mental ill health, there is no lack of suggestions for other though more minor, rôles they might assume.

Recently the Middlesex County Council asked the Minister of Health's permission to allow patients other than expectant mothers and young children to attend its municipal clinics[1] The proposal arose apparently, from a request by a general practitioner that one of his asthmatic patients should attend such a clinic for breathing exercises. The Minister it is understood would not sanction this and the *Municipal Journal* expresses disappointment at his refusal to approve a scheme which would have fostered coöperation within the National Health Service and would have eased the strain on hospital outpatient departments.

The relaxation classes which many municipal clinics hold for expectant mothers are open to the patients of general practitioners, and to hospital patients, as well as to those booked with local authority midwives Moreover, local authorities through their close association with the work of hospitals, are also interested in patients with asthma—particularly those who at the request of a hospital consultant are put under the care of a health visitor It seems reasonable then, that a general practitioner should be allowed to send his asthmatics to the welfare centre for suitable exercises

The Minister, however evidently thinks that schemes such as the one suggested by the Middlesex County Council would lead to too great a similarity between the clinics and the hospital outpatient department—diminishing their emphasis on prevention His apparent intention to keep the control and operation of physiotherapy within the hospital service may in fact be wise There is much new ground to be covered in the promotion of better mental, social, and physical health, and those who are planning the future activities of the clinics need have no lasting regrets at his refusal to let them do work which properly belongs to the hospital outpatient department

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[1] *Municipal Journal* Feb 11 195

# In England Now

*A Running Commentary by Peripatetic Correspondents*

It is a sad thought that after many centuries the natural dyes are giving ground to the synthetic products of the chemical industry It is only a matter of time, I suppose, before the lore so carefully handed down by word of mouth for countless generations is lost, for instance, there must be few people nowadays with expert knowledge of the growth and preparation of woad

Gone too are the days when dyestuffs were sent as tribute from vanquished to vanquisher Factories, industrial secrets, or atomic scientists are the modern counterpart of the insect dye kermes which the Romans exacted from the defeated Spanish tribes Oddly enough the Spanish got their dye back centuries later from the New World as cochineal, which is related to kermes and a better dye to boot Stout Cortez, who found the Aztec chief, *Montezuma, exacting it from subject tribes,* was not slow to learn from his example and bring some back to Spain He started a prosperous trade which gradually ousted the Old World dye All this only goes to prove once again that human nature is much the same the world over—whether Roman, Castilian, or Mexican Indian—and a nice splash of colour is almost a psychological necessity for our well-being

* * *

Matron has a healthy contempt for the psychs I first became aware of this when I asked if I might bring a friend, a child-guidance specialist, to see her residential home for three-to-five-year-olds Sensing a certain resistance, I did not press the issue

Apparently a few months ago, a " rationalisation " of psychs descended on her establishment Among other things, they recommended that the children should not be taught to say " please " and " thank you ", that there *should be no control over their comings and goings from* the house or grounds, and that sit-down meals should be replaced by a running buffet Matron is not prone to indecision She announced that, unless *all* the recommendations were rescinded at once, she would resign

Matron is still there, and the children remain happy, healthy, and uninstitutional—even though I am their " father figure "

* * *

All day Sunday I had been feeling off colour, shivery, myalgic, with a nagging discomfort below my right ear Monday is an early-rising morning, and at 7 A M I became conscious of the noise of the alarm, and pain below and medial to both ears simultaneously I stretched and yawned—and shut my mouth very quickly and hastily palpated my jaws After a horrified look in the mirror, I returned to bed announcing firmly that I was unfit for professional duties or domestic chores, and, no, I didn't know who was going to drive young Patrick to school

A few hours later the family doctor confirmed the diagnosis by examination from the doorway, left an insurance certificate, and asked me if I knew the complications He could be heard chuckling all the way to his car Since then I have telephoned, or been telephoned by, about half a dozen colleagues, and have had the comments of perhaps a dozen more reliably reported I have to record a high degree of sadism in the medical profession in this country This sadism may be overt, shown mainly by surgeons (" *wait till the complications get you* " theme), may be disguised as helpful advice, usually from physicians (" Heroic doses of wide-spectrum antibiotics *may* abort painful complications "), or may present as *Schadenfreude* in the uproarious Rabelaisian laughter of hearty G P s

There must be a paper somewhere in all this—but can anyone tell me, is orchitis really so *very* painful ?

* * *

I have just realised that, as an incomer to the North of England, I have been using a phrase which is open to misinterpretation by the wearers of white or red roses In seeking for the elusive inferior border of the liver and the furtive lower pole of the spleen, I have always urged my patients to breathe deeply I have *encouraged* them by uttering rhythmically the monosyllabic instructions " In ! Out ! " " In ! Out ! " I have long been puzzled by their response

Myself " In ! Out ! " Patient " No, doctor "
Myself " In ! Out ! " Patient " No, doctor "

An so on *ad infinitum*, almost *ad nauseam* The other day light broke when I heard one patient adjuring another with the well-known words, " If ever tha' doost owt for nowt, do it for thee'sen "

* * *

We are often told that there is nothing new under the sun, but it came as a shock to read in *The Boke of Knowledge* (1535) a clear description of a method developed in the late war for the estimation of specific gravity of blood

> " For to know whether ye shall die within xii months or not, let a drop of your blood fall into a dish of water, and if it descend whole into the bottom, ye shall live that year, and if not but go abroad, not "

The " dish of water " is a little disturbing, but maybe there was enough copper or other metallic contaminant *in any one area to give a reasonable result*

* * *

There can be no question that my general health has improved, because people often remark how well I look My appetite, always hearty, has increased and I have gained half a stone in weight Between meals I eat sweets No longer do I get those troublesome extra-*systoles I have no morning cough and my eyesight is,* I fancy, keener On the other hand that tendency to drowsiness in the afternoon has not abated, nor has that uninvestigated epigastric discomfort two hours after meals Poetic inspiration is at a standstill and the creative impulse sadly lacking Melancholia is profound and increasing, and evenings are so full of longueurs that, unable to read or write, one goes early to bed

Yes, I've given it up I smoked my last pipe on Jan 11

* * *

Like myxomatosis, it's getting nearer It started about three years ago in the new building estate and quickly spread to the council houses in the village Now it's all along the roads at the back of the station. It has even appeared in some of the hotels on the Beacon. The district nurses have got it, but so far the hospital and all save one of the local G P s have escaped It's in the gardener's cottage at the top of the lane My daily woman has it in her kitchen, and my 95-year old cardiac patient was one of the first victims

Having kept free for so long I thought I was immune, but my housekeeper has just told me that her television set is ordered, and " Will it be all right if the aerial is put up this week ? "

* * *

It is not often that our patients advise us how to fill in their death certificates, but I have lately been *offered* some help of this kind I may add that the patient has every prospect of surviving for some years yet, though according to his letter he has already undergone two deceases He writes

SIR,—Before making out Death Certificate *certifying* the cause of my Death, would you kindly study carefully my history of Medical and Operational also X Ray reports appertaining to my Hospital treatment which spreads over a period of years

You will note that my leg as caused me trouble from 1920 and my pensionable decease from 1917

Therefore I am of the opinion these two deceases will eventually cause my passing away, and should this be so then it is hoped that you will make out the Death Certificate to certify

(1) Leg
(2) Pulmonary Emphsema with Fibrisis Non T B

Thanking you,
Yours Faithfully,
(Signed) Late M Smith

# Letters to the Editor

## COUNTING THE SWABS

SIR,—I think the time has come when an authoritative body representative of surgery in this country should examine and declare its views on the question of the surgeon's responsibility for the swabs used during an operation. The position at present is confused. The judges are laymen and they look to the learned professions by way of expert evidence for guidance in matters which are individual to each profession.

I hold strongly to the view that the accuracy of the swab-count at the end of an operation should be wholly the responsibility of *one person*. I feel that there is danger in the knowledge of a shared responsibility and that so long as this is the case the absolute care required for safety will not always be exercised by all individuals. In my view the responsibility should be the theatre sister's (nurse taking the case). She alone knows how many swabs and packs she started with or were added during the operation and therefore she alone is in a position to make the count at its termination. It is unreasonable that a surgeon carrying out a long or difficult operation should at the same time be required to take and legally be held to share, the responsibility for the accuracy of the swab-count at its termination.

The surgeon's responsibility during an operation is in my opinion to exercise an over all supervision; the nurse's responsibility is more particular and confined. The surgeon at the beginning of the operation should satisfy himself that the system dealing with the swabs is an accepted one and that the nurse concerned has had the necessary experience. At the end of the operation he must inquire if the swab-count is correct and if it is not it is clearly his responsibility to search for the missing swab in the operation area and it is his responsibility to decide when that search should be abandoned if it is unfruitful. He should also be expected to help and coöperate with the nurse taking the case in every way possible—for example he should never take a swab direct from her table.

It is on the vexed question of divided responsibility for the swab-count that an authoritative statement is required. I submit that the obvious representative body to review this subject is the council of the Royal College of Surgeons in suitable consultation with the Royal College of Obstetricians and Gynæcologists and representatives of the Nursing profession.

London W 1  VICTOR H RIDDELL.

## DANGER OF VITAMIN K TO NEWBORN

SIR,—I wish to draw attention to the possible danger of administering unnecessarily large doses of water soluble vitamin K analogues to premature infants.

I have recently investigated a small series of cases of kernicterus and hæmolytic anæmia in premature infants whose only treatment had been relatively high doses of a water soluble vitamin K analogue ('Synkavit') for hæmorrhagic disease. There was no evidence of Rh incompatibility in any of these cases. It has since been found that administration of various water soluble vitamin K analogues in relatively high concentrations to rats can cause hæmolysis. The hæmolysis is very severe in animals on diets deficient in vitamin E, and the fact that newborn infants, in particular premature infants, are low in this vitamin may predispose them to hæmolytic disease.

Clinical and laboratory experience has indicated that doses of synkavit of the order of 5 mg per day by injection are quite adequate for treating hæmorrhagic disease of the newborn. There is however a widespread tendency to use much higher doses in the belief that this vitamin is innocuous under all circumstances. Whilst there is no evidence to suggest that serious hæmolysis occurs in conditions other than prematurity, it does seem that doses in excess of 5 mg per day by injection in premature infants, in whom low vitamin E levels are common, are unnecessary and potentially dangerous.

Clinical Pathological Laboratory
Radcliffe Infirmary
Oxford
A C ALLISON

## ISONIAZID RESISTANCE

SIR,—We wish to comment on the excellent editorial in your issue of Jan 29.

First and in particular reference was made to the observations of Katz et al.,[1] which at first sight may appear to have a bearing on the problem of pathogenicity of isoniazid resistant mutants of typical mammalian strain tubercle bacilli for human beings. We would like to add emphasis to the criticism already succinctly cited in your editorial that the 'strain' isolated from their patient was inhibited by a combination of very low concentrations of isoniazid and streptomycin in vitro:

Katz et al. were unable to account for this inasmuch as they believed they had ample evidence of total resistance to high concentrations of isoniazid alone and of streptomycin alone. Several experiments in our laboratories have shown that a population of tubercle bacilli in which all or nearly all of the bacterial cells are separately resistant to both isoniazid and streptomycin are not inhibited by a combination of low concentrations of both drugs. In culture-media containing such combinations they are inhibited only by concentrations of either drug which are inhibitory in the absence of the other drug. In other words there is no significant bacteriostatic synergism between isoniazid and streptomycin for tubercle bacilli. It is evident, therefore that Katz's 'strain' was a mixed *population of* drug-susceptible and drug resistant tubercle bacilli; probably the former organisms were masked by too large inocula in the performance of drug resistance tests.[2] It was for the purpose of avoiding such clinically important errors that methods[3] were devised for fuller quantitative investigation of the bacillary populations in sputum. It is only fair to note that these authors may have failed to take into account the fact that large challenge doses of pure populations of isoniazid resistant mutants may induce gross primary tuberculosis in normal guineapigs which regresses after the first few weeks of infection.[4,5] Be that as it may, the apparently high pathogenicity of their presumably isoniazid resistant 'strain' for guineapigs also shows that their clinical observations have no pertinence to the question as to whether or not guineapig attenuated isoniazid resistant mutant strains of tubercle bacilli are pathogenic for man.

It seems fair to conclude that the observations of Katz et al. have little to offer concerning the clinical implications of microbial resistance to isoniazid in tuberculosis.

The communication which you cited from Medical Research Council workers[6] concerned itself with the possibility that patients with resistant strains in the sputum at the time of discontinuation of isoniazid therapy might more rapidly become culture negative, or at least resistant-strain negative, "if resistant strains were less pathogenic in the environment in which they originated."

Analytically difficult problems are posed by the techniques of drug resistance tests, the possible subsequent breakdown and ulceration of lesions which harbour metabolically quiescent drug sensitive bacilli during the period of therapy, and the possibilities of reverse mutation. Aside from these there exists the basic question as to whether the clearly evident ability of catalase-negative strains to continue proliferation in the peculiar environment of the open pulmonary cavity—the environment in which they obviously originate—can really be viewed as having any import with respect to their pathogenic potentialities compared with those of the parent catalase positive strains from which they derive.

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1. Katz, S., Storey, P. B., McCormick, G. F. *Amer. Rev. Tuberc.* 1954, 70, 881.
2. Middlebrook, G. *Ibid*, p. 9[illegible]
3. Middlebrook, G., Cohn, M. L., Schaefer, W. B. *Ibid*, p. 852.
4. Karlson, A. G., Ikemi, Y. *Proc. Mayo Clin.* 1954, 29, 119.
5. Mitchison, D. A. *Brit. med. Bull.* 1954, 10, 115.
6. *Thorax*, 1954, 9, [illegible]

We have been interested in this problem and have presented some of our clinical observations in a communication to appear in a forthcoming issue of the *American Review of Tuberculosis and Pulmonary Diseases* [7] It is conceivable that too little emphasis has been placed upon the following

(1) The probability [8, 9] that isoniazid resistant, catalase negative mutants of tubercle bacilli find only in the medium of autolysing leucocytes in open cavities the dissolved catalase needed for their multiplication in vivo

(2) The fact that isoniazid can safely be administered to tuberculous patients in doses of 8–16 mg per kg per day (except in grossly obese individuals) provided pyridoxine is simultaneously administered in doses of 25–100 mg per day [10, 11] Approximately 300 tuberculous patients have been treated at our hospital on such regimens for the past year with no instance of peripheral neuropathy, and with no instance of catalase positive resistant bacilli appearing in cases initially treated on such regimens

(3) The arrest of progressive lesions in some patients upon increase in dosage of isoniazid from the range of 2–4 mg to 8–16 mg per kg per day,[12] an observation also made in several patients in our hospital This interruption of a "downhill course" in such circumstances is easily explained It may reasonably be attributed to inhibition of further multiplication of catalase positive drug-susceptible, or weakly drug resistant, organisms in individuals who acetylate the drug [13] or otherwise render it antimicrobially inactive to such a degree that the lower dosage is not actually chemotherapeutically adequate Some authorities [14, 15] still have many patients under their care "who are dying of progressive tuberculous infection with these isoniazid resistant, avirulent bacilli" while under treatment with 2–4 mg of isoniazid per kg per day perhaps dosage of the drug is important

Many intriguing phenomena make mandatory a clear definition of the problem of microbial mutation to isoniazid-resistance from the bacteriologic point of view To cite just one example, there exist morphologically or chromogenically "atypical" tubercle bacilli, isolable in pure culture from the sputa and resected lung specimens of a small percentage of tuberculous patients, which are natively at least ten times less susceptible to isoniazid in vitro and natively non-pathogenic for guineapigs Such strains in our experience are very strongly catalase-positive, and so are their isoniazid-resistant mutants The clinical significance of isoniazid resistance cannot be settled without valid qualitative and quantitative bacteriological and biochemical data Hypnotised, as it were, by the historically ominous clinical implications of drug resistance and of a persistently positive sputum, we, like many others, were foundering at the clinical level, until relationships were established between clinical dosage of isoniazid, "one step" mutation to high resistance to this agent, bacterial catalase deficiency, and attenuation for laboratory animals

In conclusion, we suggest that the pertinent question to be settled with regard to this aspect of the chemotherapy of tuberculosis may fairly be framed as follows Are isoniazid-resistant, catalase negative strains of tubercle bacilli per se attenuated for man, and, if so, in what respects ? We are very gratified to note that British investigators consider this a question deserving serious study Suffice it to remark that, presumptuous as our convictions in this matter may have appeared, further experimental studies in our laboratories with hamsters as well as with guineapigs, rabbits, and mice, and with rhesus monkeys in the Christ Hospital Institut for Medical Research at Cincinnati by Schmidt et al.,[1 have strengthened those convictions only for mice—an only for certain strains of mice, challenged by certai routes—are catalase negative strains of tubercle bacill significantly pathogenic

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G MIDDLEBROOK
S H DRESSLER

## SANATORIA

SIR,—I have followed the correspondence on th subject with some anxiety Is this advocacy of domiciliary treatment of pulmonary tuberculosis being carried too far ? Is it, perhaps, prematurely spreading to such an extent that many of our so called "country convalescent homes capable of caring for coughing consumptives" will, in the near future, be closed down converted to some other use, and irretrievably lost to the service of the tuberculous ?

Yes These "coughing consumptives" may prove to be a much bigger problem than they are at present The general hospitals will certainly not want to have anything to do with them Our present enthusiasts may regret, at no very distant date, that they burned their boats, as they are indirectly doing at this moment, before their experimental treatments have stood the test of time

Barton-on Sea,
Hampshire

R S CALDWELL.

## CLINICAL STAGING OF CARCINOMA OF THE BREAST

SIR,—Those who work among cancer patients ar be increasingly aware of the difficulties of comparing the results of treatment methods, owing to the lack of agreement about staging this disease The cervi uteri is the only site for which an international staging exists, and it is a reproach to cancer specialists all over the world that in the last twenty-five years there has until recently, been no real effort to do the same fo other sites

At the sixth congress of the Union International Contre le Cancer held in Brazil in July, 1954, the staging of carcinoma in several sites was discussed—e g, th breast, larynx, and pharynx Oddly enough, the staging of cancer of the larynx, which is a rare disease an which is treated on a large scale in comparatively fe centres, provoked long and even acrimonious discussion By contrast, breast staging was the subject of a numbe of proposals but these aroused little interest and scarcel any debate

*It seems to many of my* colleagues at the Roya Marsden Hospital (formerly the Royal Cancer Hospital that international agreement on the staging of breas cancer is more urgently required than for any other sit in the body, for the following reasons

1 The high incidence of the disease
2 The large number of clinicians treating the disease
3 To discover the effect of any one treatment upon th disease so that different methods of treatment can b compared
4 Because the comparatively high survival rate woul surely make this comparison worth while
5 Because there seems to be a more reasonable hope o achieving earlier diagnosis in cancer of the breast by appropriate propaganda than in most other cancer sites, an therefore it is important to try and find out whether suc propaganda would succeed in improving the results o treatment

No doubt the World Health Organisation is the prope body to decide the matter, and only they can effectivel advise the universal adoption of a staging which wil inevitably dissatisfy many people The next meeting o

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[7] Oestreicher, R, et al *Amer Rev Tuberc* (In the press)
[8] Middlebrook, G, Cohn M L *Science* 1953 118 297
[9] Cohn M L Kovitz C, Oda U, Middlebrook G *Amer Rev Tuberc* 1954 70 641
[10] Biehl J P, Vitter, R. W *Proc Soc exp Biol, N Y* 1954, 85 389
[11] Oestreicher R., Dressler, S H, Middlebrook G *Amer Rev Tuberc* 1954 70, 504
[12] Costellectos, E, Nassainas, A *Rev Tuberc Paris,* 1954, 18, 1091
[13] Hughes H B Schmidt L H Biehl, J P Transactions of the 14th Conference on the Chemotherapy of Tuberculosis Atlanta Ga February, 1955 In the press
[14] Schwartz W S *Ibid*
[15] Hinshaw, H C. *Ibid*
[16] Schmidt, L H, Hoffman, R, Jolly, P N *Ibid*

International Union against Cancer in London in . Is it too much to hope that before then British ons and radiotherapists may have met and discussed agreed upon a clinical staging for carcinoma of the st, so that the clinicians of this country at least can forward a basis for discussion which already mands firm support?

his letter is written in the hope of stimulating interest ction and to say that the Royal Marsden Hospital ing to take the initiative in arranging such meetings icians as would be necessary to determine this ter if no official body is likely to do so in the very future

d Marsden Hospital,
London, S.W.3

MICHAEL HARMER.

## THE LOWENFELD MOSAIC TEST

Sir,—It was pleasant to see the review of my book issue of Feb. 12. Since it appeared, however, it been pointed out to me that the impression given the review is that the test is mainly suitable for use children. I would like, therefore, to explain that is a misunderstanding as the test is of very wide cation particularly useful in consultation work. experience reported in the book is on work with normal, neurotic, and psychotic and on the of the test as a cross-cultural tool as well as for ren.

, W.11

MARGARET LOWENFELD

## RETROLENTAL FIBROPLASIA

Sir,—Ashton et al.[1] found experimentally that sure to a high concentration of oxygen was the important cause of retrolental fibroplasia. Clinical vations on premature infants have confirmed these gs, but the mechanism of the obliterative changes the retina and the nature of the stimulus which the later stages of retrolental fibroplasia forms pathol vessels, are still unknown. Taking note, however, work of Warburg et al.[2] on metabolism in the retina of the investigations of György et al.[3] into the special res of the metabolism of growing organisms it is ble, I think, to deduce something of the pathogenesis.

burg showed that the retinæ of frogs, rabbits, and rats a high rate of anaerobic glycolysis. György et al. found the lactic-acid levels in the blood (an index of the degree olysis) are higher in premature infants than in full-term s, and higher in full-term babies than in older infants. er we have found, using Warburg's apparatus, that the of anaerobic glycolysis in the kidneys of suckling rats is r than in adult rats. Warburg pointed out (a) that obic glycolysis diminishes or disappears when the oxygen y increases, and (b) that growth is impossible without lysis.

m these facts it follows (a) that anaerobic glycolysis ntial to the retina and must be maintained (this is ially necessary in growing organisms with a high rate of obic glycolysis), and (b) that if the oxygen tension rises normal, the retinal arteries of a premature organism ract to reduce the oxygen supply. In more mature isms in which the retina is fully developed and in which rate of glycolysis is much lower this reaction does occur because in them the oxygen increase is not so rous. Constriction of the retinal vessels impairs the ion of the retina and ultimately damages it. Vascular ing and the formation of connective tissue are secondary which appear when the organism returns to a normal en concentration.

is hypothesis, which is shortly to be published[4] in er detail, explains why the effect of oxygen in causing retrolental fibroplasia is proportional to the degree of immaturity of the retina, to the duration of exposure to oxygen, and to the concentration of oxygen.

Brunswick, Germany

TH. BREHME

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[1] hton, N., Ward, B., Serpell, G. Brit. J. Ophthal. 1953, 37, 513; Ibid, 1954, 38, 385, 397, 433.

[2] arburg, O., Negelein, E., Posener, K. Biochem. Z. 1924, 152, 09. Ibid, 1925, 165, 192.

[3] örgy, P., Brehme, Th., Brabdy, M. B., Kelker, W., Jb. Kinder eilk. 1927, 118, 178. Ibid, 1928, 120, 42. Biochem. Z. 1928, 08, 3.6.

[4] ch. med. Wschr. (in the press).

## ESCHERICHIA COLI IN INFANTILE DIARRHŒA

Sir,—Since June, 1952, we have been investigating the relationship between *Escherichia coli* and infantile diarrhœa. Some of our findings have already been published in your columns.[1 2] This letter deals with the results obtained from the start of our investigation to the end of March, 1954.

The infants investigated were from the infants' home of our university here in Nagoya. Approximately equal numbers of male and female infants were included, all under two years of age, and most of them more than six months old. All were artificially fed. Antibiotics were used in 1952 because of the severity of the disease, but since then the cases of diarrhœa have been mild, and antibiotics have not been given.

Rectal swabs were investigated for *Esch. coli* O-111 B4 and O-55 B5 from June, 1952, onwards, O-26 B6 from October, 1952, O-86 B7 from August, 1953, O-25 from July, 1953, O-44 from September, 1953, and O-102 from October, 1953. Usually the fæces were examined weekly, but during epidemics more frequent examinations were made. The results are summarised in the accompanying table.

No *Esch. coli* O-111 B4 were isolated in 1952, and all cases related to this strain occurred in 1953. *Esch. coli* O-55 B5 were isolated from the start of our investigations, and in 1952 there were two epidemics in the home which were related to this strain.[1 2] After the epidemics of 1952 *Esch. coli* O-55 B5 were isolated occasionally, *but in smaller numbers*, and there was a period of about four months in 1953 during which they were not isolated at all. *Esch. coli* O-26 B6 were isolated mainly in the summer of 1953.

*Esch. coli* AND INFANTILE DIARRHŒA

| Strain | No. of cases in which isolated | Severity of disease | Relationship between *Esch. coli* and diarrhœa | | |
|---|---|---|---|---|---|
| | | | Definite | Doubtful | None |
| O-111 | 11 | Severe<br>Moderate<br>Mild | 0<br>0 } 5<br>5 | 0<br>1 } 3<br>2 | 3 |
| O-55 | 29 | Severe<br>Moderate<br>Mild | 4<br>[illegible] } [illegible]<br>11 | 0<br>1 } 2<br>1 | 3 |
| O-26 | 13 | Severe<br>Moderate<br>Mild | 0<br>1 } 6<br>5 | 0<br>1 } 3<br>2 | 4 |
| O-86 | 27 | Severe<br>Moderate<br>Mild | 0<br>3 } 10<br>7 | 0<br>3 } 9<br>6 | 8 |
| O-25 | 3 | Severe<br>Moderate<br>Mild | 0<br>0 } 1<br>1 | 0<br>0 } 1<br>1 | 1 |
| O-44 | 14 | Severe<br>Moderate<br>Mild | 0<br>0 } 0<br>0 | 0<br>2 } 7<br>5 | [illegible] |
| O-102 | | Severe<br>Moderate<br>Mild | 0<br>0 } 0<br>0 | 0<br>0 } 1<br>1 | 4 |

A close relationship between the bacilli and the infantile diarrhœa was observed with the three strains O-111 B4, O-55 B5, and O-26 B6.

The relationship of *Esch. coli* O-86 B7 to infantile diarrhœa was first noticed by Braun[3] in Heidelberg. In our investigations this strain was isolated in large numbers in 1953, and was the strain most frequently isolated that year. A close relationship between it and the disease was observed.

A relationship between *Esch. coli* O-25 and infantile diarrhœa was first noted by Ocklitz and Schmidt[4] in [illegible]. Our observations seem to confirm their findings [illegible] need more evidence before we could draw valid conclusions Similarly, we are continuing our investigations on *Esch coli* O–44 and *Esch coli* O–102

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[1] Ogawa, T., Ogawa, J. *Lancet*, 1952, i, [illegible].
Ogawa, T., Ogawa, J. *Ibid*, 1952, [illegible], 1244.

[3] Braun, O. H. *Fortschr. Med.* [illegible]

[4] Ocklitz, H. W., Schmidt, E. [illegible] 1953, [illegible], p. 106.

It should be noted that there were cases in which no relationship was established between the strain isolated and the occurrence of diarrhœa The proportion of such cases was 27% in *Esch coli* O–111, B4 cases, 16% in O–55, B5 cases, 30% in O–26, B6 cases, 30% in O–86, B7 cases, and 33% in O–25 cases On the other hand, 50% of the O–44 cases, and 80% of the O–102 cases, were unaffected by diarrhœa due to these strains

Last year we also cultured *Esch coli* from the infants' fingers, toys, diaper covers, and bed sheets, and from the rails of their beds The strains isolated were those commonly found in the fæces at that time

It was noted that almost all newly admitted infants became infected with *Esch coli* soon after admission—usually within three months The strains isolated were those most prevalent at the time Those observations suggest that the infection was spread by contact, but spread by droplet infection cannot be excluded, since the prevailing strains were obtained from nasal swabs taken from the infants

During the two years of our investigation different strains of *Esch coli* predominated In 1952 O–55, B5 was isolated in large numbers, and apparently caused two epidemics, but *the organisms decreased in number during 1953, when* O–86, B7 became the most prevalent strain O–111, B4, which was not detected in 1952, appeared occasionally in 1953 *In severe epidemics, the strains which were isolated* usually belonged to one definite group, but in a sporadic outbreak many different strains were isolated simultaneously Infants who stayed for long periods in the home became infected with several strains in turn—e g, one infant was infected with O–55, B5 in July, 1953, with O–111, B4 in September, and with O–86, B7 in November of the same year

TOHRU OGAWA
JIRO OGAWA
Nagoya City University,
Japan

## SICKLE-CELL TRAIT IN SOUTH TURKEY

SIR,—Last week's interesting article by Dr Aksoy on the sickle-cell trait in Turkey links the Eastern Mediterranean with Greece, Italy, and (what may not be generally known) with Portugal in this respect On a recent visit to Portugal I was interested to hear from Prof Carlos Trincão that some of his patients with sickle cell anæmia come from an area to which in the 18th century African slaves were sent to help in the drainage of swamps

Miss Cutbush and I did not want to suggest that the sickle cell trait was introduced into Africa by Indian tribes No doubt we must take some responsibility for this misunderstanding, since it occurs so often in the literature I have discussed this misunderstanding elsewhere [1]

The sickle cell trait is found in India and in Africa, but the common link is the finding of sickle cells in the Veddoids of South Arabia Elsewhere [2] I have given the reasons for which this ancient stock seems to be the most likely source of the gene (apart from the possibility of its arising by independent mutation) Features common to Africa and to India may have come across the Indian Ocean in either direction, or may have filtered along the southern fringe of the Asiatic continent, entering or leaving Africa by land in the north east, yet others, such as certain customs connected with cattle and milking cults common to the Todas of South India and to the Hottentots of South Africa, are likely to have their origin in Mesopotamia whence they made their way both to India and to Africa It has been suggested that the Veddoids of Arabia are the remains of greater numbers whom the arrival of the desert climate drove forth to India, if there was such a centrifugal dispersal it might well have driven some to Africa, and there is even reason to believe [3] that they may also have spread into the Mediterranean region

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H LEHMANN

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[1] *S Afr J Sci* 1954 51, 140
[2] *Eugen Rev* 1954, 46, 101
[3] *Man*, 1953 no 5

## ESTIMATION OF MERCURY IN ATMOSPHERE

SIR,—In the course of further work in our laboratorie on methods of analysis for mercury in atmosphere an biological tissues, considerable variation in the result of recovery experiments was found when the metho used in the investigation by Bidstrup, Bonnell, Harvey, and Locket [1] was checked

A modification of the method for estimating mercur in atmosphere is described below, and it is recommended that the earlier method [2] be abandoned Th conditions necessary to avoid fluctuation in results mus be so strictly controlled that this method in its origina form is unreliable for routine use

While the figures in the paper by Bidstrup et al indicate that mercury was present in the atmospher of the workshops, we consider that they do not give reliable indication of the amount of mercury present The accuracy of the method for estimation of mercur in urine is satisfactory

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P LESLEY BIDSTRUP
D G HARVEY
J A BONNELL
R DREW
E KING
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Oldchurch Hospital,
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### MODIFIED METHOD

*Principle*

A known volume of the atmosphere to be tested is draw through a bubbler containing acid permanganate solutio This procedure extracts the mercury from the atmospher and is the method of trapping described by Kuziatina.[3]

In the method described by Buckell [2] the permangana solution is decolorised by adding oxalic acid solution an warming Investigation showed that this procedure fo decolorising gave unreliable results It is now recommende that the permanganate be cleared with hydrogen peroxid *solution and the use of this reagent is the chief innovation*

The mercury which has been trapped in the solution i determined by an extractive titration procedure which is modification of the method by Buckell [2]

*Reagents*

Trapping solution potassium permanganate, 0 05 N in 5 sulphuric acid

Decolorising reagent 20 volume hydrogen peroxide solutio

Dithizone (diphenylthiocarbazone) stock solution 50 m % *w/v* in chloroform

Dilute dithizone solution for use dilute stock solution 1 *100 with chloroform for immediate use giving a 0 5 mg % w* solution

Stock standard mercury solution solid mercuric chlori 0 06767 g is dissolved in glass distilled water and the solution ma up to 100 ml This gives a solution of concentration 500 μg Hg per ml

*Dilute standard mercury solution* the stock standard mercur solution is diluted 1 in 100 with glass distilled water to give a solutio of concentration 5 μg of Hg per ml

All chemicals AnalaR grade

*Apparatus*

Glass bead bubblers are used

*Method*

The method is essentially an extractive titration Th bubbler is washed out with glass distilled water, the solutio decolorised with 10 ml of hydrogen peroxide solution, and th *sample transferred to a separating funnel*

Dithizone solution is added from a burette, in small amount and after each addition the two layers are mixed by shaking the funnel The orange red lower layer of mercury dithizonat is run off and titration continued until a final addition o dithizone, after shaking, remains blue green

A calibration graph is constructed with known amounts o mercury, plotting millilitres of dithizone solution agains microgrammes of Hg The volume of dithizone solutio required to titrate an unknown sample can then be equate to its mercury content On the above strengths, 1 millilitr of dilute dithizone solution is approximately equivalent to 2 μg of mercury Full details have been submitted fo publication [4]

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[1] Bidstrup P L Bonnell J A, Harvey, D G, Locket, S *Lancet* 1951 ii 856
[2] Buckell M *Brit J industr Med* 1951 8 181
[3] Kuzlatina N S *Zarodskaya Lab* 1939 8 174
[4] Drew R G King E Unpublished results

## RUPTURE OF LAPAROTOMY WOUNDS

SIR,—It was disturbing to read Mr Standeven's estimate (March 12) that wound dehiscence may take place after up to 7% of all abdominal operations Mr Standeven deserves credit for having placed the facts before us, though few modern surgeons would accept his figures It is, however, surprising that this entirely preventable catastrophe should be regarded with the complacency formerly accorded to pulmonary embolus

A "burst abdomen is always due to failure of the suture technique before the tissues have healed sufficiently to withstand intra abdominal tension The time taken for tissues to heal is usually unknown, hence a suture should ideally last for at least a month The weakest part of the abdominal wall is the midline, and the only layer worth considering for strength is the aponeurosis It should surely not be beyond our resources to ensure that this is held firmly together for four weeks

There are four common techniques involving either continuous or interrupted stitches and absorbable or permanent material Interrupted sutures would at first seem stronger than a continuous stitch, but experience shows that where the tissues are poor there may be such necrosis within the constriction of each suture that the stitches cut out and allow the wound to open; with the continuous suture there is virtually no tissue deprived of its blood-supply by constriction all round. Against the continuous suture on the other hand, is the fact that it must withstand a strain inversely proportional to the number of bites of tissue taken in closing a wound of standard length. This surely rules out catgut as a safe suture material since its absorbability may vary between wider limits than those specified by the manufacturers.

The ideal material would appear to be a strong unreactive material that may be left permanently in the tissues and I have personally had the greatest satisfaction from the use of monofilamentous nylon I commenced using no 5 (black) but I now use a continuous suture of no 7 (purple) and I believe that with ordinary care I shall entirely abolish postoperative wound disruption I have had one failure due to my own carelessness in tying a poor knot and trimming the ends too short, but this is unlikely to happen again I must also report an incidence of 1% of sinus formation leading down to the knot at one or other end I regard this as a small price to pay for the complete safety from wound disruption and herniation but I am hopeful of finding a way of securing the ends of my continuous suture that will be free from the risk of this minor and uncommon complication

Birmingham　**WILFRID MILLS**

SIR,—Mr Standeven's article is a valuable contribution to this important subject I would like to emphasise the significance of his observation that bursting of the abdomen is always accompanied by an ooze of serous fluid which is often bloodstained

In many cases the wound has broken down completely before the skin sutures are removed protrusion of the viscera being prevented *only* by the *skin* sutures. The apparently sound apposition of the skin edges at the time of removal of the sutures may mask the serious underlying condition Only too often in these cases there is sudden protrusion of intestine during the day after the skin sutures have been removed

In general the occurrence and degree of visceral protrusion determine the mortality of this dangerous complication of abdominal surgery All house-surgeons and nursing staff should be taught that a serous exudate especially if bloodstained from a clean stitched abdominal wound indicates rupture When such an exudate is observed the skin sutures should be removed in the operating theatre and the underlying defect immediately repaired

Mr Standeven cites an estimated incidence of incisional hernia of 4%[1] With vertical incisions in the upper abdomen the incidence is probably very much greater Cosbie Ross and Walsh[2] in a follow up of a series of cases of partial gastrectomy, found incisional hernia in 11 of 9 cases examined

The incidence of burst abdomen and particularly o incisional hernia is far too high and is a reproach t surgery

Dublin.　**ANTHONY WALSH**

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[1] Romanis W H C, Mitchiner P H Textbook of Surgery London, 1937, vol II p 602

[2] Ross, J C, Walsh A. *Postgrad med J* 1949 25 469

## A SHARED RESPONSIBILITY

SIR,—Your leader of last week is timely It shoul be remembered that responsibility for patients alread in our charge is in no way lessened by the necessit to admit others Premature or precipitate discharg may result in medical or social crises or both whic have unfortunate but justified repercussions on—o from—patients and their friends In such cases th terms uncoöperative ' and "difficult' are ofte misapplied to the patient and his family but in fac they describe only too aptly those of us who fail to pla in time for adequate social arrangements to be made

As Miss Sheridan points out when time and opportunity are given for constructive planning and adjustment discharges can usually be arranged which ar satisfactory and acceptable to all concerned Indee experience of this type of shared responsibility' demonstrates that *earlier* discharges are in some case possible

The sharing of responsibility can only become a everyday practice where contact between medical staf patients their friends, and the social services is clos throughout treatment

West Middlesex Hospital
Isleworth.　**MARJORY W WARREN**

## YELLOW PHOSPHORUS POISONING

SIR—Dr Caley and Dr Kellock in their very interesting account of a case of yellow phosphorus poisonin (March 12) ignore two very important points of toxicology the second of which probably explains the wide variatio in clinical lethal doses

These points are (1) route of absorption (I take fairl large amounts of sodium fluoride daily but take great ca that none shall enter my respiratory system) (2) vehic of administration (an attempt to poison Rasputin wit cyanide failed on account of the sugar used to mask th dose—a very heavy one)

In the case described a woman of 71 there would be very little ability to digest fats ability to digest fats wanes with age except in the Eskimo who have evolved a race of fat digesters because fat was the only pure form of energy food available to them The patient took the phosphorus on bread and butter and would likely spread the butter thickly t mask the taste; the yellow phosphorus, being strongly fat soluble would mostly remain in the unabsorbed fat and do no harm. I have pointed out[1] that this also happens with the fat-soluble vitamins and this is an important cause of the frequency and lethality of respiratory infections in th older population

Now though 600 mg was ingested, how much was absorbed is quite another matter As I have pointed out,[1] if I ingest an egg I may acquire 80 calories of energy or fewer calories than that or may actually lose calories by combating putrefaction of the undigested egg or by the voiding it by vomiting

My purpose is not in any way to disparage the account or the treatment given which probably saved th patient's life, but to point out that lethal doses ar described in individual cases which vary from 60 to 400 mg this means that survivors have ingested (but not absorbed) varying amounts between these extremes and in the present case 600 mg is said to have been ingested There must therefore be some other factor than ingestion and this factor in some cases at least will be the vehicle of administration—i e., the fats in the food and in the intestine which elderly people in temperate and hot climates are progressively less able to split and absorb

Bitton, near Bristol.　**A T TODD**

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[1] Todd A T Good Living. Bristol 1952

## RABIES IN GERMANY

SIR,—Your annotation of Jan 1 mentions reasons why the vaccination campaigns applied successfully in four specified countries are not applicable to conditions in Western Germany  Since the Malayan campaign is one of those cited, and since it would appear that at least one reason adduced for non-employment of similar methods in Germany is false, you will, perhaps, permit me to comment

It is doubtful whether full, critical, and unbiased consideration has been given to the rôle that mass vaccination of the dog population can play in a country faced with a serious rabies epizootic  Six reasons are given why vaccination of dogs in Germany has been rejected  They are

1. *That wild animals are chiefly affected* —This of itself is not an argument against the vaccination of dogs, or, for that matter, of cats or cattle, all of which can be successfully immunised [1]  There is no evidence that in Germany the infection in wild animals constitutes a serious threat to man  it is probable that infection in human beings would be more likely to result from the bites of dogs or cats than from those of foxes, badgers, deer, wild boars, cattle, or squirrels  If, then, the vaccination of dogs and cats can very largely prevent the transmission of the disease to man it is not immediately obvious why vaccination has been rejected as a control measure

2 *That cats are considered more dangerous than dogs* —The cat is not usually regarded as an important vector of the disease  Since, however, cats can be effectively immunised against rabies with chicken-embryo vaccine (Flury strain),[1] it is curious that their vaccination does not seem to have been considered

3 *That police measures have been successful in the past in controlling infection in dogs* —It is apparent from the references cited in your annotation [2,3] that police measures are no longer as reliable or as adequate in the particular circumstances of the moment as they are reported to have been in the past  I have had some experience of the seeming reluctance of certain Continental veterinary authorities to accept the vaccination of dogs as the powerful prophylactic weapon that it has proved to be [4–7]  Whilst the vaccination of dogs, even using the more modern vaccines, is not necessarily the main feature in any rabies control programme, there is increasing evidence that, when rigidly applied, it can succeed where conventional police sanitary measures have failed [8–9]  To reject the vaccination of dogs as a control measure in a country seriously infected with disease is hardly consistent with the resolution adopted in the 22nd session (1954) of the committee of the Office International des Epizooties [10] on which the German authorities were represented  The resolution states that in a seriously infected country strict police sanitary measures should be applied together, where necessary, with the preventive vaccination of all dogs aged 3 or more months by means of an officially controlled vaccine of proved innocuity and antigenicity

4 *That vaccinated dogs must still be controlled, because their saliva is infectious, even though they are protected against clinical development of the disease* —This is a most remarkable statement and one, I suggest, that should be viewed with the greatest reserve  It implies that a carrier state in dogs is induced by vaccination and, apparently, on a general scale—a finding that is, in my view, quite new  Zunker [11] states

> ‘ Il y a assez de rapports à notre disposition pour prouver que les chiens vaccinés peuvent contracter la rage malgré la vaccination avec du virus fixe et qui ils peuvent propager la maladie  Ils ne l ont pas fait parce qu'ils sont tombés malades au *stadium prodromorum* et non pas au *stadium irritationis* et ainsi la maladie a été difficilement décelable  La salive de tels animaux a été examinée et trouvée infectieuse

This is a somewhat different state of affairs from that quoted in your annotation  It is not unlikely—indeed, it is highly probable—that such animals were vaccinated when in the incubative stage of the disease  this is a not unusual finding in any vaccination campaign although it may be less likely to occur with chicken embryo vaccine (Flury strain) than with a vaccine of the Semple type [7]  Zunker's statement cannot be accepted as a condemnation of vaccination  there is too much evidence to the contrary

5 *That the public would be less likely to coöperate in other control measures if dogs were vaccinated* —This must remain a matter of opinion  It was certainly not the case in the 1952–54 control campaign in Malaya  The purpose of mass vaccination was, prior to this campaign, explained through every possible publicity medium, and the reasons for its being made compulsory were made abundantly clear  Public coöperation was most gratifying  A total of over 115,000 dogs was vaccinated in the whole of the Federation of Malaya during 1954, representing not less than 85% of the total dog population  The last recorded case in a dog was in June, 1953—i e, 20 months ago

In any rabies control campaign it is essential that adequate legislation exists to counter every move of those who, for one reason or another, attempt to evade this measure designed to protect human beings from an exceedingly unpleasant death  Legislation, even though it may have to be draconian, must be backed by an official determination to enforce it  Half-measures are unlikely to succeed  It is, perhaps, significant that the successful vaccination campaigns in the four countries quoted in the annotation—Hungary, Israel, Japan, and Malaya—were all *compulsory* ones

6 *That the cost and effort in vaccinating all dogs would be very great* —If a charge is made for vaccination a rabies control campaign need cost the authorities very little  One of the most promising of the newer vaccines—the chicken embryo vaccine (Flury strain)—is produced on a large scale only in America, and its purchase would, of course, involve dollars  An alternative would be to use a potency tested nervous tissue vaccine injected intramuscularly, as recommended by W.H O [1]

The effort required must be balanced against the benefits that may accrue  From the point of view of the protection of human beings there can only be one conclusion

Office of the Director of Veterinary Services,
Federation of Malaya,
Kuala Lumpur

C W WELLS

## EPIDEMIC VERTIGO

SIR,—The case-reports of epidemic vertigo uncomplicated by oculomotor palsy—e g, Dr Leishman's (Jan 29) cases 3 and 5, and possibly 2 correspond, as regards history, signs, and progress, to the vestibular neuronitis described by Hallpike [12] and Dix and Hallpike [13]  If caloric tests of vestibular function are carried out on patients with vestibular neuronitis when the acute symptoms have subsided, it is found that function is absent or deficient on one or both sides  Since loss of vestibular function usually persists in spite of symptomatic recovery it is not too late to carry out caloric tests on Dr Leishman's cases, and on those reported by subsequent correspondents

It would be a pity if two terms, implying the existence of two separate clinical entities, were introduced for what may be one and the same condition  May we perhaps look forward to hearing from your contributors regarding the results of caloric vestibular-function tests in their cases ?

Dulwich Hospital,
London, S E 22

BERNARD FREEDMAN

SIR,—It is doubtful if Dr Leishman's “epidemic vertigo” with oculomotor complication constitutes a new entity, or his substitution of this term for “acute labyrinthitis” an advance of ætiological significance

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1 *Tech Rep Wld Hlth Org* no 82, 1954
2 Zunker M *Bull Off int Epiz* 1954 **42** 83
3 Ruppert F *Ibid* p 70
4 Meyer K F *Bull Wld Hlth Org* 1954 **10** 856
5 Vittoz R *Bull Off int Epiz* 1950 **34** 37
6 Kaplan M M Goor Y, Tierkel, E S *Bull Wld Hlth Org* 1954 **10** 743
7 Wells C W *Ibid* p 731
8 Brückner A L *Proc U S live Stk sanit Ass* 1946, **50** 37
9 Korns R F, Zeissig A *Amer J publ Hlth* 1948, 38, 50
10 *Bull Off int Epiz* 1954 **42**, 857
11 Zunker M Office international des epizooties report no 354 to the 22nd Session 1954

12 Hallpike C S *Congr int Oto rhino laryng* London 1949, vol 2 p 514
13 Dix, M R, Hallpike, C S *Proc R Soc Med* 1952, 45, 341

The cases described by him appear to comprise two elements: (*a*) a Ménière component (sudden onset of vertigo accompanied by vomiting with or without spontaneous nystagmus and tinnitus) and (*b*) the sphenoidal sinus syndrome (occipital or retro-orbital headache vertigo, and tinnitus) The oculomotor involvement is the commonest of the ocular palsies in sphenoidal sinus disease where the sinus pneumatises the greater wing of the sphenoid Since on Dr Leishman's own cognisances the epidemic' qualification is not really adequately supported, it is a pity that the otherwise full investigations were not accompanied by a nasopharyngoscopic one, and catheterisation and lavage of the sphenoidal sinuses with full examination of the "returns"

Cape Town, South Africa. M GLASS

## OSTEO-ARTHRITIS OF LUSCHKA JOINTS

SIR,—Dr E J Crisp's theory of the causation of root pain in the arm (Feb 5) makes very interesting reading Of more practical value in the treatment of this very common disabling condition would be an account of his technique of neck traction" which in his experience almost always affords relief

Idutywa Transkei
South Africa. D C G COOPER

*** This letter has been shown to Dr Crisp who writes "Neck traction is best given with the patient in the recumbent position and may be carried out manually or by weights and pulley using the Sayre's sling The important point in technique is correct posturing of the neck, for if the cervical spine is extended most of the pull will be applied to the trachea and œsophagus. Hence, if we wish to stretch the capsular ligaments of the joints of Luschka traction is given with the neck in a moderate degree of forward flexion while if it appears that the symptoms arise in the zygapophyseal joints the neck is flexed still further forward When posterior marginal lipping is severe enough to give rise to electric shock like feelings in the legs if the neck is suddenly bent forward, the object of treatment will be to increase the range of cervical extension so that the spinal cord will come to lie more posteriorly in the thecal canal Traction is therefore given with the neck in the neutral or slightly extended position In all these cases the poundage employed will vary from 25 lb to 45 lb for a duration of upwards of 15–20 minutes treatment ing given daily until relief is obtained

## INNOCUOUS TEMPORARY IMMOBILITY

SIR,— Rhodesian Doctor' rightly draws attention his letter last week to the *questionable diagnosis* Miss Peace's attacks Nurses more than printers those in other occupations frequently describe condi ons other than the immobility, which I have dealt ith elsewhere

The case of the sleep paralysis described by Rhodesian Doctor, accompanied by sleep hallucinosis an auditory nature is of a type less common than that ccompanied by visual hallucinations but episodes irresistible sleep without structural lesions are more kely to be due to 'idiopathic narcolepsy especially sleep hallucinosis is frequently associated with that ondition

Although without a detailed psychological analysis each case no denial of conflict can be made it would ar to be absent in instances in which fear is unlikely have occurred such as that of a man unable to move prevent his supper from burning over the gas or of ook-out who saw a ship clearly but could not report it many cases among nurses the subject has been unable rise to meet a senior member of the staff so that the nce of unconscious fear cannot be excluded but in one case a man could not move when his relief, junior to him, came

"Rhodesian Doctor" is not quite right in reporting that I would prefer to call the condition 'innocuous temporary immobility' In view of many conditions, such as standing to attention, being also states of innocuous temporary immobility the condition can be described as 'an innocuous temporary immobility," but it is inaccurate to omit the indefinite article.

Bristol G DE M RUDOLF

## JAUNDICE

SIR —According to my reckoning, there are 35 causes of jaundice and it is not surprising that the diagnosis is sometimes obscure

In an effort to clear my own mind, I have tried—on paper—to evolve a diagnostic plan However, pencil and paper are poor substitutes for experience and as the acquisition of experience consumes both time and lives I should like to submit my premises and conclusions to the criticism of your readers.

*Premises*

1 Medicine can offer specific treatment in those types of jaundice which are due to a spirochæte or a rhesus anomaly In all other cases it can offer supportive and symptomatic treatment

2 Surgery can offer an almost certain cure in acholuric jaundice a probable cure in calculous jaundice, the chance of a cure in postoperative or congenital stricture, and the hope of a cure in malignant obstruction

3 Calculous jaundice is nearly always intermittent hardly ever deep and progressive

4 The administration of a general anæsthetic to a patient with infective hepatitis is a disaster and operation on a jaundiced patient is fraught with the danger of postoperative anuria

5 Radical pancreatico-duodenectomy is open to the following objections

(*a*) Its mortality rate is high, and many of the dead patients might have been given a valuable lease of life by a short-circuit.
(*b*) Its cure-rate in cancer of the head of the pancreas is very low
(*c*) Operable carcinoma is not easily distinguished from chronic pancreatitis.

*Conclusions*

1 The normal approach to a therapeutic problem—that of basing treatment on an accurate diagnosis—has disadvantages in a jaundiced patient because the difficulties of diagnosis tempt both physician and surgeon to use exploratory laparotomy as a diagnostic instrument This hazard can be minimised if we reverse our normal processes of thought and attempt to narrow the diagnostic field by a system of exclusion rather than by one of selection In jaundice more than in any other disease, one should ask oneself the question Is this operation really necessary?

The following types of case should *not* be operated on:

(*a*) Children (acholuric jaundice and congenital stricture excepted)
(*b*) Young adults with deep and progressive jaundice
(*c*) Mild or transient jaundice unless associated with the clinical and radiographic features of gall stones.
(*d*) Patients with evidence of related disease in other parts of the body (e.g cancer of the stomach bowel or breast enlargement of the spleen [except in acholuric jaundice]; ascites; œsophageal varices)
(*e*) The old and decrepit the drowsy the hiccupping and those with oliguria or anuria—because operations on the dying serve no useful purpose

2 If the original list of 35 starters is consulted, it now seems that very few runners are left They are as follows:

(*a*) Suspected congenital or postoperative strictures, which will demand exploration.

(b) Suspected acholuric jaundice, which the laboratory will confirm

(c) Transient or fluctuating jaundice, with the clinical and radiographic features of gall stones

(d) Deep and progressive jaundice in a middle aged or elderly patient, fit to withstand a major operation. It is in this type of case that liver function tests have their main, and possibly only, practical value If they, and needle biopsy, do not distinguish between infective hepatitis and obstruction of the bile duct, we are left with

3 The only finisher, a middle aged or elderly patient, deeply jaundiced for a month, fit for major surgery, and with equivocal liver-function tests One must now resort to the last court of appeal, exploratory laparotomy, and the following procedure is suggested

Make a short Kocher incision under local anæsthesia If the liver has the appearance of infective hepatitis (and I should be glad to know if a "typical" appearance exists) or contains deposits of cancer, close the abdomen. If the gall bladder is distended or diseased, give a general anæsthetic, extend the incision, and perform a laparotomy If the findings suggest a stone impacted in the ampulla, remove it, if they suggest carcinoma of the head of the pancreas, or chronic pancreatitis, perform a short circuit, if they suggest carcinoma of the ampulla, carry out a radical pancreatico duodenectomy An alternative to the "short Kocher" is to buy a peritoneoscope

South Mimms Hertfordshire V J DOWNIE

## ENURESIS

SIR,—Dr Poulton, in your last issue, refers to the combination of physical causes which in his view give rise to enuresis, and then says that "waking, restriction of fluids, drugs, and the nocturnal bell-ringing device" "must be brought to bear" on them

Even if all were agreed about the ætiology of enuresis, the effect of such treatment on the child needs further thought The child is as unaware of having too small a bladder, and too much urine, as he is of emotional tension He knows that he wets the bed and has mixed feelings about it—most of these reflecting the adult's attitude towards it If he is unaware of the cause, punishment will seem to him unjust If he feels guilty, punishment will increase his guilt There is no evidence that children accept being wakened, having bells rung at night, and being deprived of fluids with any better grace than an adult would accept these things On the contrary, such management must tend to emphasise their helplessness—a state of affairs which breeds resentment

Whatever we believe the cause of enuresis to be, we agree that punishment in itself will not cure it What punishment will do, however, is to concentrate the child's attention both on the deed and on the surrounding sentiment Whether disapproval of this dis ease is expressed by caning or being wakened several times every night, to the child the cruelty will appear the same

It is not far fetched to believe that, having unconsciously done something of which the adult disapproves, the child in turn resents the adult's behaviour Legitimate revolt not being part of his privileges, he is driven further along the road of suppressed anger Whether his bladder capacity later improves or not, his earlier treatment will have left indelible marks on his character

London, S W 15 HEDY SYMONDS

SIR,—In your leading article on enuresis (Feb 19) you mention an electric alarm which wakens the enuretic patient as soon as micturition starts In patients in whom night incontinence is due to imbalance between the sleep depth and bladder sensation, the alarm works by establishing a conditioned reflex over a period of days or weeks

Various patterns have been described from time to [illegible] compact apparatus is now available in this country It consists of a small metal box containing dry battery, an alarm "rattle," an indicator bulb, and switch Perforated aluminium-foil pads are used whic are soft, malleable, and of the consistency of thin canvas These are placed beneath the patient, separated by a ordinary draw sheet, and covered by a similar sheet Th alarm operates with as little as 2 ml of fluid

This apparatus, the 'Chiron' nocturnal enuresis alarm is marketed by Messrs Down Bros and Mayer & Phelps 32, New Cavendish Street, London, W 1

London W 1 D F ELLISON NASH

## EFFECTIVE CIRCULATION OF UTERINE WALL IN LATE PREGNANCY

SIR,—The remarks by Mr Morris and his colleague (Feb 12) on the cause of the sudden onset of pre eclampsia interested me very much

In recent years a lively discussion has arisen abou hyperfunction of the adrenal cortex as a possible facto in the genesis of toxæmia of pregnancy

Browne[1] in 1944 remarked that it had not been determine whether the adrenal cortex played any part Novak[2] ha stated *"the tendency towards salt and* water retention i probably caused, partly by an increased function of th adrenal cortex, which is generally markedly enlarged i pregnancy, and partly by the amounts of estrogen and progesterone produced in the maternal organism"

I have put forward the following hypothesis[3]

During pregnancy the adrenals are hyperfunctioning, to meet the needs of the fœtus The permeability of the mother's capillaries is affected by the increase in cortical hormones, and the effect is to encourage retention of sodium and water Adrenal cortical and medullary function are interrelated, a we know from Addison's disease, if no cortical hormone are produced, noradrenaline cannot be synthesised In pregnancy the quantity of disposable cortical hormones i increased, and so too will be the quantity of noradrenaline. The greater part of these hormones are stored in the gland, to be later released by some "trigger mechanism" and caus œdema, and also hypertension as in phæochromocytoma Phæochromocytoma has often been found in cases of toxæmia. One of the best provocative tests is intravenous injection of 0 005 mg of histamine, after which the blood-pressure rise to 300 mm. Hg Could the same thing occur spontaneously where there is no phæochromocytoma but only hyperfunction of the adrenals, in which the greater part of the gland's secretions have been stored ?

Clearly, Nature does not like histamine, the end product of allergic reaction, circulating freely in the maternal blood, for the histaminolytic power of the maternal serum steadily increases, and the same is true of that other product of antigen antibody reaction—acetylcholine—for cholinesterase also increases during pregnancy, especially in cases of toxæmia[4] Should some histamine escape destruction, then the cortical and medullary adrenal hormones are suddenly released, causing œdema and hypertension By constriction of th arteries the placental circulation is diminished The antigen giving rise to rhesus incompatibility passes through th placenta from the fœtus to the mother, and the antibodie back from the mother to the fœtus, probably materna histaminase (produced in the maternal part of the placenta also passes to the fœtus Mostly the result of an antigen antibody reaction—histamine—will be destroyed, but no and then it may escape, causing release of adrenal hormone which in turn are responsible for œdema and vasoconstriction infarcts of the placenta are formed under the influence o noradrenaline If this working hypothesis is right, then Rh incompatibility should be commonly accompanied by toxæmia This is in fact so, not only when Rh incompatibility manifests itself as hydrops fœtalis and placentæ, but also is icterus gravis and its sequel, anæmia neonatorum When after birth histaminase is lacking, histamine escapes destruction and can cause release of adrenal hormones It is probable tha cortical mineralocorticoids control the passage of sodium through the wall of the erythrocytes and eventually hæmolysis; the reduction of available histaminase at birth may explain the onset immediately afterwards of icterus gravis.

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[1] Browne, F J *J Obstet Gynæc., Brit Emp* 1944 51, 438
[2] Novak E *Amer J Obstet Gynec* 1937, 34, 237
[3] Schuurmans D *Med Tijdschr Geneesk* 1950, 94, 319, Zb *Gynäk.* 1953, 75, 241
[4] Hofbauer, J *West J Surg* 1941, 49, 615

In the light of this working hypothesis I administer anti histamine substances in toxæmia of pregnancy and Rh incompatibility

Amsterdam.  R Schuurmans

## INACCURACY IN THE LABORATORY

Sir,—It is gratifying to note, from your annotation last week, that freeze dried samples of blood-serum will soon be available for use as standards in hospital laboratories. But one wonders to what extent this will be effective in localising the sources of error in clinical biochemistry, and in remedying them

The international survey to which you referred [1] was conducted with similar material and this was available to all laboratories in this country Yet only a few participated Besides, detailed analysis of the problem [2] has shown the matter to be complicated by a number of factors, not the least being the degree of skill and the psychological condition of the analyst. Further work [3] has shown that the standardisation of proprietary brands of laboratory reagents may leave much to be desired, while some of the techniques employed do not stand up to critical scientific appraisal

What does seem desirable is a thorough overhaul, sibly at the national level to involve analytical thods standardisation of reagents, laboratory equip nt, and personnel Would the clinical value of the laboratory results warrant such an effort? What is the position with regard to the other branches of clinical pathology?

Area Pathology Laboratory
Westwood Hospital
Beverley Yorks  O Bassir.

## MASKED EPILEPSY

Sir,—I am glad that Dr Kempton (Jan 22) commented on Dr Wallis's paper on masked epilepsy (Jan 8) It is of course well known that there are various unusual manifestations of epilepsy such as sudden attacks of abdominal pain, sudden vomiting and psychomotor equivalents I agree with Dr Kempton, however, that it is going altogether too far to suggest that epilepsy is an important cause of cyclical vomiting, headaches night terrors, unexplained fever, personality disorders pains in various parts of the body and even the so-called three-month colic I can see not the slightest connection or resemblance between for instance three month colic and epilepsy

I found Dr Wallis's case records unconvincing The two cases of so-called cyclical vomiting were certainly *not* typical of that condition and the association with unconsciousness suggests that the diagnosis was something else perhaps epilepsy Dr Wallis does not mention the mode of onset in his case-histories. For instance headache of gradual onset would not make one suspect epilepsy headache or other pain of very sudden onset might

It is well known that acute infection with fever may precipitate fits in an epileptic (apart from the so-called febrile convulsions) and that elevation of temperature may result from a severe major convulsion That *is* another thing however from saying that attacks of fever may be manifestations of epilepsy

I am similarly unconvinced by the finding of an abnormal electro-encephalogram In the first place very few of us physicians are competent to interpret electro-encephalograms. We have to rely on someone who knows how to interpret them. Abnormal electro-encephalograms can be found in otherwise normal persons, such as relatives of epileptics and in children with fever as a result of an acute infectious disease The finding of an abnormal electro-encephalogram in patients with vomiting surely does not prove that the vomiting is due to epilepsy After all, epilepsy is common. So are cyclical vomiting headaches three month colic abdominal pain and personality disorders, and it would be surprising if some epileptics did not have some of these conditions.

It would be a tragedy if all children with cyclical vomiting and the other conditions mentioned were deemed to be epileptics If general practitioners accepted Dr Wallis's thesis, the hospitals would be inundated with requests to investigate these cases for epilepsy

Department of Child Health
University of Sheffield  R S Illingworth

Sir,—Having read Dr Wallis's article and his reply (Feb 20) to Dr Millichap's letter (Feb 19), I want to add that we saw in our clinic about four months ago a patient with cyclical vomiting and a patient with periodic symptoms who had received several forms of treatment without benefit We concluded that these might be instances of masked epilepsy and we began treatment with phenobarbitone which has proved successful. We hope soon to publish these cases along with the electro-encephalographic findings

Gureba Hospital,
Istanbul Turkey  O A Ulutin

## TREATMENT OF CHRONIC AMŒBIC DYSENTERY

Sir,—In his article on the Treatment of Chronic Amœbic Dysentery with Antibiotics in Combination with other Drugs (March 12), Lieut Colonel Inder Singh says:

Usually gr 4 of emetine will quickly control an acute attack of amœbic dysentery but the amœbic cysts are not affected. Again later in the article, he states

Since then aureomycin and oxytetracycline have been found to combat the secondary infection and to destroy both the trophozoites and the cysts"

One gets the impression that the destruction of cysts is an important aim in treatment. This misapprehension is prevalent even among physicians with a wide experience of tropical diseases In reality it is pointless to consider treatment to destroy harmless cysts whose presence in the fæces is merely indicative of the existence of an infection of the bowel wall with amœbæ Destroy the amœbæ and cyst production ceases Despite assertions to the contrary it is by no means certain that any drug given by mouth destroys cysts within the lumen of the bowel it is much more probable that such a drug would destroy trophozoites, thus preventing further formation of cysts with consequent disappearance of the latter from the fæces

Calcutta.  C B Andrade

## HOSPITAL REPORTS FOR INDUSTRIAL MEDICAL OFFICERS

Sir,—In common with many other industrial medical services it is the practice in this department to examine all employees who have had accidents or serious illnesses or operations before they resume duty Most of them have attended hospital either as an outpatient or inpatient.

Obviously it is vitally important for us to have a clear history of what has happened what diagnosis has been made and what treatment given before we can assist in the patient's full rehabilitation by giving him a suitable job The patient is seldom able to supply this information and never with accuracy Therefore we obtain his consent and write for details to his general practitioner who almost without exception is extremely courteous and coöperative Although this help is willingly given, it must be an infernal nuisance for the doctor (possibly at the end of a long day) to dig out hospital reports, and often write further details and send them to us

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1. Proceedings of the 1st European Congress on Clinical Chemistry Amsterdam 1954
2. Bassir O *Ass clin. Biochem. Newsletter* 1954 2, 10
3. Bassir O Unpublished.

I suggest therefore that hospital consultants and their assistants could help considerably by asking their patients What is your occupation? Has your firm an industrial medical service? Will you agree to a report on your condition being given to your company's doctor? If this is done a copy of the report issued to the general practitioner could be sent to the industrial medical officer, and it would save a great deal of work and speed up full rehabilitation

It should of course be indicated on the general practitioner's report that a copy has been sent So many of our good friends now automatically send us a copy of reports when they sign their patients off, and one wants to save them unnecessary work

Medical Department,
British Railways, Southern Region,
London S E 1

L J Haydon

## HOSPITAL STAFFS

Sir,—For several years your correspondence columns have carried *cris de cœur* from senior registrars about the shortage of consultant posts Many suggestions have been made, including increasing the number of such posts and decreasing the number of senior registrarships Although both these measures would go some way towards improving the position, the remedy would at best be only temporary and at worst might increase the present difficulties within a few years, as well as being extravagant in public money There is a different aspect of this question which is not often enough considered

When the generation of consultants now retiring made their choice of specialisation as against general practice, most of them knew that their career would be lengthy and at first economically crippling They needed either considerable faith or large private means Many of them sacrificed in the first ten years after qualifying the opportunity for marriage and having a family If they failed to make the grade their outlook was much as it is today But their numbers were restricted without the necessity for artificial control, since only determined and confident men were prepared to face the risk

Since the war, and particularly since the start of the National Health Service, the whole emphasis of medicine has shifted to the hospitals The first ten years of a specialist's career have been made feather bedded and easily accessible to many who would formerly have been put off by the financial hardships Every increase in the salary of junior hospital staff exaggerates this tendency, and will ultimately increase the number of senior registrars competing for consultant posts.

This is not to say that the tendency I am criticising has been entirely bad Junior hospital staff can lead fuller, easier, and perhaps eugenically better lives The discrimination in favour of those with private means has been eliminated Unfortunately the sacrifices and struggles of the early years have not been eliminated also they have been deferred until later on in life This cannot be a healthy tendency A man approaching middle age should be able to look forward to reasonable financial security The right time for struggling is when you are young

I feel very strongly that when the next pay increases are made (politicians nowadays refer to "change in the rate of rise of the cost of living" as if it were an inevitable process) they should be made in such a way as to help the young entrant into general practice The lure of the hospital and consultant ladder is quite great enough already It is at present often more profitable for the man qualified, say, for three years to go into hospital rather than into general practice The work is easier, and the hours and conditions better It is silly to say that one job is more worth while than another Both are necessary—though the country could spare registrars more easily than general practitioners The decline in the status of general practice is an artificial one, capable of correction.

The view that junior hospital staffs are perhaps over- [illegible] that is often expressed in your columns For obvious reasons it is not likely to be a popular one None the less I feel that it needs stating It sounds priggish from the mouth of a registrar and complacent from the mouth of a consultant, and equally unconvincing from either I write therefore as one who has benefited from and appreciated junior-hospital staff pay, who is not at present contemplating entry to general practice, who is in a good position for unprejudiced thinking—and who dislikes unsigned letters

London S W 1

C J Dickinson

Sir,—I am amazed by the solution to the senior registrar problem suggested by Mr McCarthy last week

The "really worthy senior registrar" would have an additional letter (E) to his title, and an extra £200 a year He would, of course, continue indefinitely to do work virtually equivalent to a consultant's, as at present, with never any hope of assuming full clinical responsibility

In Mr McCarthy's scheme the newly graded men are to be at the disposal of the hospital boards for "duties throughout the region" I take this to mean that they will be directed from peripheral hospital to peripheral hospital in the region concerned, as and when difficulties of staffing in the junior grades arise They might even occasionally be working near their home and have a chance to see their family, for, as Mr McCarthy himself points out, these men do have families

Should some such solution be accepted, the problem would be considered solved once and for all

The present acute concern about "the plight of senior registrars," arises presumably from the increasing difficulty of junior grade staffing of peripheral hospitals I submit that the real cause of this difficulty is the awareness among the younger men of the hopeless struggle of non teaching hospital senior registrars in recent years to obtain a permanent post in their own specialty

If the reason for the shortage of consultant posts is, as we are sometimes given to understand, a financial one, then I would offer the following simple suggestions

(1) Give the senior registrars who have completed their training, and who receive adequate recommendation from their chiefs, a small number of consultant sessions in a hospital group Even three or four sessions would do provided (2) below is also granted

(2) Allow them to make up for the other sessions with whatever private practice they can obtain in competition with other consultants

Senior Registrar.

## DIAGNOSIS OF ACTIVE CARDITIS

Sir,—In the course of investigations on rheumatic carditis, one of us (G C) noted that the electrocardiogram (E C G ) of a patient with rheumatic fever showed a peculiar change following the administration of digitalis, after no more than an average therapeutic dose, the P–R interval increased to an extent normally observed only after toxic doses, and even then but rarely This observation suggested to us that the peculiar sensitivity to digitalis of patients suffering from carditis (already alluded to by some authors) might prove of diagnostic value

We therefore gave 0 8 mg 'Cedilanid' (lanatoside intravenously to 34 patients with rheumatic carditis, a to a control group of 82 people with neurocirculato asthenia

The results supported our hypothesis a significant del in the P–R interval was observed in 10 out of the 34 patien with rheumatic carditis The E C G s began to show chang $^1/_2$–1 hour after the injection. These reached a maximum oft as late as 24 hours after the injections and the changes lasted f 1–2 days The delay in conduction was 0 16 sec in 2 cases, a 0 10 sec in 2 other cases, and it exceeded 0 03 sec in every cas On the other hand, this effect was observed in none of the people in the control group This alteration in the E C G m therefore be a sign of active carditis, and this is supported the fact that the changes were observed only during the acti phase of the disease Tests carried out after recovery were negative in every case the P–R interval remaining unaltered.

As far as we are aware, this test has not previously been used in the diagnosis of rheumatic carditis without articular manifestations

II Medical Clinic,
University of Szeged
Hungary

G CZONICZER
R SZABÓ

## HYPOTHERMIA IN THE NEWBORN

SIR,—I was fortunate in hearing Dr Trevor Mann speak on this subject at the Royal Society of Medicine and was very much interested in his letter last week.

Three factors may contribute to the syndrome in varying degrees—namely cold surroundings immaturity, and infection Where the weather is sufficiently severe the second and possibly the third may be absent

The condition is almost wholly preventable and its appearance is surely a reproach to us all Earlier generations took their babies to bed with them in cold weather when the babies ran the risk of being overlaid. Doctors midwives, and health visitors have preached the dangers of this *practice*, and of hot-water bottle burns without emphasising the need *for constant warmth* Consequently we now see infants who have become cold in icy bedrooms and when their condition deteriorates, are insulated in layers of blanket before being brought into the warm living room

Since a discussion last year with Dr Mary Fisher of the Oxford health department, I have seen no case from the city during the present winter She has made sure that every midwife and health visitor in Oxford instructs the mothers under her care Our scheme whereby a health visitor comes into the maternity wards each week provides another opportunity to reinforce this teaching and inquire about the coal position at home

Treatment of the established syndrome is still a matter for discussion and it is difficult for any one individual to see a sufficient number of comparable cases to speak dogmatically Discussions with those who are dealing with experimental hypothermia in animals have revealed a number of fresh problems Nor must we forget that in neonates, new methods of treatment may produce unexpected long term changes—e.g , oxygen therapy in premature infants Do we yet know whether the premature baby's cerebral cortex is unaffected by prolonged cold ?

Finally, is this a new syndrome ? I suspect that Sparta had a name for it

Radcliffe Infirmary
Oxford

VICTORIA SMALLPEICE

SIR —Dr Trevor Mann asks if others have seen any examples of hypothermia in the newborn

Those who see infants born outside hospital must surely be familiar with the clinical picture he describes and I, for one have carried a low reading thermometer for some years as these cases do not seem to be rare in the cold months of the year

My experience has in most respects been similar to his in that babies over 5½ lb weight at birth are often affected and the appearance of the children is as he describes but most of the cases in this district have had some degree of sclerema as well as œdema. This sclerema may be slight, only a *few* small areas, usually on the legs or buttocks, being affected but this change has also been extensive

During the recent cold spell 4 examples have been seen and the largest number seen at one time was 5 in a fortnight, towards the end of the hard weather in 1947 The story has usually been the same—namely that the family has run out of coal This happened in the case of a small private maternity home some years ago 2 infants a few days old were being nursed in a small unheated room Both had pronounced œdema and sclerema and they recovered

A clinical impression notoriously to be mistrusted has been that these infants all œdematous who had red cheeks and often red extremities also had some infection In each of the 2 cases for which necropsy records are available hæmorrhagic pneumonia was found The prognosis has been far from hopeless, since more than half the infants have survived and by no means all have been admitted to hospital Dr Mann is no doubt right in advising against too rapid heating of these infants In 2 cases I probably made this mistake 1 died after four days following rapid warming and in the other the worst yet encountered (the infant was so stiff with sclerema that the body could be raised like a board, by one finger placed underneath the back), rapid heating led to temporary improvement followed by death after sixteen hours and hæmorrhagic pneumonia was found post mortem

Recently cases of sclerema, some apparently examples of the syndrome under discussion have been reported from America In these recovery has apparently been facilitated by the use of corticotrophin The condition in that country is thought to be very rare, and one wonders whether the much greater use of central heating and the larger number of deliveries in hospital may be the cause of this. In 3 of my own patients corticotrophin has been used, with recovery in 2 and death in the 3rd described above

With children who have such a low vitality infection must always be imminent and admission to a hospital ward may be dangerous unless every precaution against cross infection is taken

Henoch in *Lectures on Children's Diseases 1889* translated by John Thomson and published by the New Sydenham Society devoted a chapter to sclerema, originally described by Underwood in the 18th century, and differentiated this condition from "œdema of the newborn." This latter condition corresponds closely to the syndrome of hypothermia of the newborn He emphasised the low body temperature noted the complications of pneumonia and convulsions, and described a case complicated by nephritis He recognised that both sclerema and œdema could co-exist in the same patient

A useful service has been done by Dr Mann in drawing attention to this condition, but I do not believe that it is a new syndrome

Wolverhampton.

H EVERLEY JONES

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# Parliament

## Obscene Publications Bill

IN the House of Commons on March 15, Mr ROY JENKINS moved that leave be given to bring in a Bill to amend and consolidate the law relating to obscene publications The measure, he said, had been drafted by the committee set up under the *auspices of the Society of Authors* of which Sir Alan Herbert and later Sir Gerald Barry was chairman The motion was agreed to and the Bill was given a *formal first reading*

## QUESTION TIME

### Heat Treatment of Milk

Replying to a question Mr HEATHCOAT AMORY, the Minister of Food said that in the year ended September 1954, about 87% of the milk supplied by retail in Great Britain was [illegible] to heat treatment compared with about 69% in [illegible]

### *Leprosy in England and Wales*

*Replying to a question* Mr MACLEOD said [illegible] also there were 161 notified lepers [illegible] special hospitals for them, one near [illegible] near Chelmsford Essex

## Medicine and the Law

### An Overlooked Swab

IN the Queen's Bench division on March 15 judgment was given in favour of a plaintiff who claimed that a swab had been negligently left in her abdominal cavity at a surgical operation.

On Jan. 7, 1953, the plaintiff was successfully delivered of a child by cæsarean section at a private nursing-home. From the evidence it appeared that the surgeon, before sewing up the peritonium, had removed those packs which he could see and for the rest relied on the formal count of used and unused packs made aloud by the theatre sister. In fact one of the packs, 10 inches square, was left in the plaintiff's body. The plaintiff sued the surgeon, the assistant surgeon, and the proprietors of the nursing-home for damages for negligence. At the conclusion of the evidence the judge ruled that there was no evidence of negligence against the assistant surgeon, and he was released from the case.

Mr. Justice Pearson said that on the balance of probabilities there had been an error in the counting; on that finding there was negligence on the part of the theatre-sister, and that negligence was a cause of the pack remaining in the plaintiff's body. Therefore the nursing-home was liable.

As to the surgeon's liability, it had been submitted that it would have been sufficient for him to show that he had acted in accordance with a recognised school of opinion in his profession, and that, although he had a duty to take reasonable precautions to ensure that no pack was left in the plaintiff's body, he had fully performed his duty by relying solely and exclusively on the sister's count of the packs. His Lordship found that it was not proved that that was in accordance with any approved practice. If Spencer Wells forceps or some other precaution were not used, the surgeon, when removing the packs, should make some mental effort to remember where he had put them. Even if that finding were wrong, in the circumstances of the present case, he would hold that it was a negligent practice in an operation of routine nature, although there might well be emergency operations where different considerations would apply. The sister's count was fallible and needed some other precautions, and the fact that the other precaution was also fallible was not sufficient reason for not adopting it. Two good, though fallible, precautions, if both were applied, would achieve a high degree of safety. The sister's count was a secondary thing, a check on something the surgeon had already done. There was therefore negligence on the part of the surgeon also. Both the theatre sister and the surgeon had failed in their respective duties. If either duty had been performed the mishap would have been prevented. The responsibility should be divided equally between them.

Judgment was given for the plaintiff for £3000, and judgment for the plaintiff's husband for £1146 special damages.

### A Death from Tetanus

A boy of 15 fell off his bicycle and lacerated his elbow. He was taken to hospital, where a doctor stitched the wound, prescribed systemic penicillin, and ordered an injection of anti-tetanus serum. This order was subsequently cancelled when the boy told a nurse that he had six months earlier received an injection against tetanus from his own doctor. The boy was admitted to hospital six days later with symptoms of tetanus; on the eighth day, despite intensive treatment, he died.

At the inquest it transpired that the earlier injection had in fact been penicillin, not anti-tetanus serum. Replying to the coroner, the hospital doctor agreed that the ideal solution would be to verify patients' statements by making inquiries from their own doctors; in practice, however, this would tend to delay the patient's treatment. He had withheld anti-tetanus serum because, had the boy's statement been correct, there would have been a risk of causing a severe reaction.

The coroner drew the jury's attention to the fact that patients who are given an injection seldom know what is being injected. He suggested that hospitals should, except in cases of life and death, always take steps to verify patients' statements. The jury, returning a verdict of accidental death, added a rider to this effect.[1]

## Obituary

### MAX NEUBURGER

M.D. Vienna

THE history of medicine, as a continuous, detailed, and documented narrative, has for a century and a half been almost a prerogative of Germanic writers. This German period began with the magnificent work of Kurt Polykarp Sprengel, completed in 1803, and ends with the recent death in Vienna of Max Neuburger.

Neuburger had all the requisites of a great historian of medicine. He was well trained, had good experience in clinical medicine and scientific research, had great facility in acquiring languages, and enormous industry, and understood well the method and importance of documentation. Eminent though the German school of medical history has been, it cannot be said that many of its members possessed literary skill or charm. Here Neuburger stood out from the beginning. He wrote simply, clearly, and well, so that all his works are most readable. His two largest productions are of the highest importance. First was the great three-volume *Handbuch der Geschichte der Medizin*, which he edited in conjunction with his gifted and genial colleague Julius Pagel of Berlin. It was completed in 1905 and must long remain as the most comprehensive work of its kind. Second was his two-volume *History of Medicine*, of which the last part was published in 1915. Most of it was later translated into English. He was the author of a multitude of other learned, delightful, and useful communications, the value of which was acknowledged by the volume of essays presented to him by his admirers in 1948 on his 80th birthday.

Neuburger, who had years before established a school and institute of the history of medicine in Vienna, was appointed full professor in 1917, and taught there actively till he was 70 in 1938. In that year, with the Nazi outbreak in Austria, he had to leave and came to England. The Wellcome Historical Medical Museum gladly found a place for him and he continued, almost without interruption, in his output of works of learning. He refused to leave London during the war and, when he was long past 70, he underwent a grave operation during the blitz and recovered well from it. In 1948, at 80, he went to live with one of his sons in the United States. Important publications continued to come from him, but, in 1952, at 84, he determined to return to Vienna. Until his death he remained, by general consent of all who have any knowledge of the subject, the most important historian of medicine in the world.

C.S.

### CHARLES RUSS

M.B. Lond.

Dr. Russ, who died on Feb. 26 at the age of 78, received his medical education at St. Mary's Hospital. In the preclinical years he showed particular ability in physiology, and after qualifying in 1903 he made a special study of the response of bacteria to electrical currents. His observation that, in a suitable suspension, there was a selective migration to one electrode was published in the *Proceedings of the Royal Society*. He went on to apply the working principle of migration to clinical conditions in gonorrhœa by a technique described in a book published in 1916. The method was also used with some success in the treatment of indolent varicose ulcers. He was given facilities for this work at St. Peter's Hospital, and later on he developed the results of his researches in private practice.

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[1] *Shrewsbury Chronicle*, March 4, 1955.

# Notes and News

## PRESCRIPTION OF TETRACYCLINE

THE Ministry of Health Department of Health for Scotland and Ministry of Health and Local Government Northern Ireland, have arranged for tetracycline to be available on prescription from April 4 The Medical Research Council has informed the health departments that tetracycline is suitable for treatment of the same conditions as aureomycin and oxytetracycline (terramycin)[1] and its toxicity is also similar so the same precautions should be observed in its administration

## ONCHOCERCIASIS

EPIDEMIOLOGICAL surveys in Africa and in the Americas have shown that in some regions of both continents 80–100% of the population are infected with onchocerca. Because of ocular complications, onchocerciasis is of considerable social and economic significance. The first report of the Expert Committee on Onchocerciasis[2] is likely to prove a landmark in the evolution of our knowledge of this disease Workers have been investigating it for twenty five years; and this report shows how much and how little we know and wisely guides the thoughts of those working in this field to the work that should have priority Some parts of the report are already outdated The meeting was held in 1953 and since then—in 1954—another meeting has been held at Léopoldville In the intervening period quite a lot has been uncovered and many of the errors at the first meeting were corrected at the second Probably the most valuable sections of this first report are those on control of the vector and of the parasite. The recommendations here are admirably expressed and solid with conviction and sense The two annexes—the first by H. T Dalmat describing the method for testing susceptibility and resistance of larvæ of simuliids to insecticides, and the second by J P McMahon on methods of estimation of river discharge for control of simuliids by D D T—are excellent They will remain as standard works for a long time

## NUTRITION RESEARCH AT COONOOR

THE report for 1953–54 of the Nutrition Research Laboratories at Coonoor South India, is a record of varied activities by the twenty three graduate members of the staff Part of the work, especially that on food analyses and field surveys, is essentially of local interest. But fundamental research is being carried out over a wide range of subjects. The body composition of a small group of healthy Indian men has been determined in respect of water content cell-solids, and fat. Resting oxygen consumption was found to correlate more closely with the estimate of cell solids than with surface-area as conventionally measured Cell-solids or the lean body mass would appear to be a more valuable unit for expressing standards of basal metabolic rates than any other at present in use.

The rates of urinary nitrogen excretion by a group of men after a simple meal of about 1200 Calories and 25 g of protein were higher if the protein was of animal origin than if it was of vegetable origin. With animal proteins nearly 50% of the excess nitrogen was excreted in the first three hours; the delay with plant proteins could be interpreted as showing a lag in their absorption and hence their subsequent utilisation.

In a study of the liver in rats on diets deficient in protein calories, pyridoxine, and choline either separately or in various combinations, the findings are being correlated with the histological picture of the liver in children in South India with nutritional œdema (kwashiorkor) Comparison of the liver pictures in nutritional œdema and experimental protein deficiency revealed many similarities although they were not identical.

Further field studies have shown that vitamin $B_{12}$ exerted no growth promoting effect on South Indian children living in a residential institution either before or after improvement in the diet

This report shows that Coonoor retains its place as a leading nutrition research laboratory The staff are clearly not short of ideas, and have the ability to follow them up

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[1] See *Lancet*, 1954, ii 820

[2] First Report of the Expert Committee on Onchocerciasis *Tech. Rep Wld Hlth Org* 1954 no 87 H.M. Stationery Office. Pp 37 1s 9d.

### University of London

The degree of PH D in the faculty of medicine has been awarded to H H. Khalil and A H Kitchin

Mr H F Cook PH D senior lecturer at the Middlesex Hospital Medical School has been appointed to the university readership in physics at the school.

### University of Sheffield

Dr Q H Gibson has been appointed to the chair of biochemistry

Dr Gibson was educated at Repton School and Queen s University Belfast. He graduated M.D with honours in 1941 and has since taken the degrees of M D PH.D and D.SC from Belfast. From 1941 to 1947 he was demonstrator and later lecturer in physiology at Queen s University Belfast He came to Sheffield in 1947 as lecturer in physiology and has since been appointed senior lecturer and recently reader in physiology Last year he joined the editorial board of the *Biochemical Journal*. His published work has dealt chiefly with problems of hæmoglobin

Dr W Whitaker has been appointed senior lecturer in medicine and Mr D H Randall and Mr D J Robertson part time clinical teachers in surgery

### West London Medico Chirurgical Society

Sir Russell Brock has been awarded this society s triennial gold medal.

### Institute of Dermatology

*Chesterfield Medal*.—Essays submitted for this award should reach the secretary of the institute, Lisle Street London W C 2 by Sept. 30

### Association of Psychiatric Social Workers

This association is to hold its annual general meeting at the Middlesex Hospital, London W 1 on Saturday April 2 at 2.30 P.M Dr John Bowlby and Prof. R M Titmuss will open a discussion on Prevention in the Mental Health Field.

### College of General Practitioners

*Butterworth Gold Medal*.—This medal is to be presented annually to the college by Messrs. Butterworth & Company medical publishers, for an essay not exceeding 10 000 words, written by a member or associate of the college on a subject connected with general practice As the subject for 1955 the council has chosen the influence of home conditions during the first five years of life on the physical and mental health of children. Essays must be submitted to the chairman of the awards committee of the college 14 Black Friars Lane London E C 4 by Sept 30

### Devon and Exeter Medico-Chirurgical Society

On Thursday March 31 at 4 30 P.M Mr J W Cook F.R.S., principal of the University College of the South West will open an exhibition of medical art and history in Exeter which this society is holding at the Royal Albert Memorial Museum, Queen Street Exeter during April (open 1.30–5 30 P M daily) The exhibition has been arranged by Mr Norman Capener and will include some classics of medical literature from the library of the Cathedral Church of St Peter and the Exeter Medical Library documents relating to old Exeter hospitals from the archives of the city and portraits and documents from the early years of the Royal Devon and Exeter Hospital.

### Royal Society

The 25 newly elected fellows of this society include Dr A W Downie professor of bacteriology in the University of Liverpool Dr K. J Franklin professor of physiology in the University of London at St Bartholomew s Hospital Medical College; Sir Harold Himsworth secretary to the Medical Research Council Mr A. F Huxley assistant director of research in physiology University of Cambridge Mr O F Lowenstein D.SC Mason professor of zoology and comparative physiology University of Birmingham; Mr A G Ogston, D PHIL. lecturer in biochemistry University of Oxford; Mr Guido Pontecorvo PH.D reader in genetics University of Glasgow Mr J A Ramsay PH D lecturer in zoology University of Cambridge; and Mr G P Wells SC.D., professor of zoology in the University of London at University College

On Thursday June 16 Prof C H Best F.R.S., of the University of Toronto is to give the Croonian lecture to this society at Burlington House London W 1 He will speak on dietary factors in the protection of the liver kidneys heart and other organs in experimental animals—the lipotropic agents.

### Long-term Effects of Nuclear Explosions

Science for Peace is holding a public conference on this subject at Holborn Assembly Hall, John's Mews, London, W C 1, on Saturday, March 26, at 2 P M

### Edinburgh Medical Exhibition

Prof D M Dunlop will open this exhibition at the Assembly Rooms, George Street, Edinburgh, on Monday, April 25 at 11 30 A M The exhibition will remain open till April 29

### Royal Army Medical Corps Funds

The annual general meeting of the members of the Funds will be held at 11, Chandos Street, London, W 1, on Monday, April [illegible] at 5 P.M.

### Inst[illegible]ançais du Royaume-Uni

On Thursday, March 31, at 8 P M, at the institute, Queensberry Place, London, S W 7, Dr B L Halpern will speak on Le Problème de l'Allergie

### World Health Day

On World Health Day, which is being celebrated in this country on April 5, Mr Iain Macleod, the Minister of Health, will open a public meeting at 5 P M at the London School of Hygiene and Tropical Medicine, Keppel Street, W C 1 Prof G Macdonald and Prof, J M Mackintosh will also speak

### Whittington Clinico-Pathological Society

The first meeting of this society will be held on Friday, April 1, at 5 15 P M, at the Archway wing of the Whittington Hospital, London, N 19 Further particulars may be had from Dr Arnold Bloom, the hon secretary, St Mary's Wing, Highgate Hill, N 19

### European Society of Cardiovascular Surgery

The fourth congress of this society will be held in Copenhagen from July 28 to 29, during the week of the International Society of Surgery The subject chosen for discussion on July 28 is Surgical Treatment of Chronic Pericarditis, and on July 29 a symposium on Angiology will be held with the International Society of Surgery The subjects of communications and discussions must be sent before April 15 to the secretary general, Dr G Arnulf, 41, rue Sainte Helène, Lyons, France The local secretary is Dr A Gammeltoft, København Amts Sygehus, Copenhagen

### Industrial Health Advisory Committee

The first meeting of this committee was held on March 18 The committee is to advise the Minister of Labour and National Service on measures to further development of industrial health in work-places covered by the Factories Acts The members include Prof R E Lane (Royal College of Physicians), Dr J A L Vaughan Jones and Dr L G Norman (British Medical Association), Dr R S F Schilling (Association of Industrial Medical Officers), Dr R Nightingale (Association of Certifying Factory Surgeons), Dr T Bedford (British Occupational Hygiene Society), and Dr R S Aitken (Committee of Vice Chancellors and Principals of the Universities of the United Kingdom)

CORRIGENDUM *Association of Surgeons of Great Britain and Ireland*.—The annual meeting in Glasgow in April will be held under the presidency of Prof C F W Illingworth, and not, as we announced last week (p 628), of Sir Clement Price Thomas, who will be *nominated* as president at the meeting

The Juan Perón prize (about £25,000) has been awarded to Prof René Leriche

Sir Ernest Gowers chairman of the National Hospitals for Nervous Diseases, has been elected president [illegible]sis Society

1127

## Births, Marriages, and Deaths

### BIRTHS

CARSTAIRS.—On March 5, to Jean (née Dutton) wife of Captain J R L Carstairs, R.A M C B.M H, Up Park Camp, Kingston, Jamaica—a son (Andrew James)

## Diary of the Week

MARCH 27 TO APRIL 2

### Monday, 28th

MEDICAL SOCIETY OF LONDON 11, Chandos Street W 1
8 30 P M Dr J T Ingram, Dr C Allan Birch C
Manifestations of General Disease
MANCHESTER MEDICAL SOCIETY
9 P M (Medical School) *General Practice* Dr Sylvia
Gastro-enteritis in Infants

### Tuesday, 29th

INSTITUTE OF DERMATOLOGY, St John's Hospital Lisl
W C 2
5 30 P.M Dr P M F Bishop Steroid Therapy
MANCHESTER MEDICAL SOCIETY
8 P M *Surgery* Prof Oscar Scaglietti (Florence) C
Dislocation of the Hip

### Wednesday, 30th

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's In
W C 2
3 45 P M Dr I Stretton Young Degeneration in
Pathology (Erasmus Wilson demonstration)
UNIVERSITY OF LONDON
5 P M (St Thomas's Hospital Medical School S E 1) P
Nickerson SC M (Winnipeg) Specific Inhibi
Adrenergic Responses
ROYAL SOCIETY OF MEDICINE 1, Wimpole Street W 1
8 P M *Pædiatrics* Dr Hugh Jolly Mr G H Mac
Dorothy Russell Hydrocephalus of Infancy
ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE 28,
Place W 1
3 30 P M Mr Joseph Minton Prevention of Blindness i
and Childhood
MANCHESTER MEDICAL SOCIETY
4 30 P M Dr Robert Forbes Recent Developments in
Litigation

### Thursday, 31st

ROYAL COLLEGE OF SURGEONS OF ENGLAND
5 30 P M Prof Lambert Rogers Vascular Diseases in
to *Otolaryngology*
ROYAL ARMY MEDICAL COLLEGE, Millbank S W 1
5 P M Dr Bernard Schlesinger Indications for
Therapy in Pædiatrics
INSTITUTE OF DERMATOLOGY
5 30 P M Dr W R Bett Medical Writing

### Friday, 1st

ROYAL SOCIETY OF MEDICINE
5 30 P M *Anæsthetics* Dr T C Gray, Dr C F Scurr
Hypothermia

## Appointments

FOUNTAIN J R., M B Edin, M R C P E senior registrar a
in general medicine, United Leeds Hospitals
SCHOFIELD, T L, CH M Lpool F.R C S consultant surge
clinical area
SHEMILT, PHILIP M B Lond, F R.C S surgical co
Military Hospital Tidworth
SMIDDY F G M.B Leeds, F R C.S senior registrar a
in general surgery United Leeds Hospitals

**Sheffield Regional Hospital Board**

ASCROFT N O M B Lpool whole time asst chest p
Wathwood Hospital, Wath on Dearne near Rother
BRITT, R G M R.C.S, D M R D part-time consulta
logist, Leicester H M C
COLLINS, JOHN, M.B Lpool whole time senior casual
Derbyshire Royal Infirmary
FAHY THOMAS M B N U I whole time asst chest p
Grimsby area
JAMES, N E, M B Lond F R C.S consultant or
surgeon main centre, Grimsby
KINSELLA, JOHN L R C P I D M R T whole time as
therapist radiotherapy centre, Derbyshire Royal I
MEJZNER STEFAN M R C.S whole time asst chest
Lincoln area and deputy physician superintendent
Hall Hospital Branston
NAPIER, J G M B Edin, F R C S E M R C O G c
obstetrician and gynæcologist, Scunthorpe and
War Memorial Hospital, and Glandford Hospital Br
RENYARD, H H M B, M S Lond, F R C.S part time
surgeon, Nottingham General and Newark Hospit
WILKINSON, J B, B.M Oxfd whole time asst chest
Lincoln area

**Birmingham Regional Hospital Board**

ELLIOTT J R, M R C.S F F A R C.S, D A part time
anæsthetist, Wolverhampton group
HOLMES J MACDONALD M D Leeds, F.R C P part-
sultant neurologist West Bromwich group
LASZLO, T J M D, D P H Prague whole time asst ge
*Birmingham (Dudley Road) group*
ROAF, ROBERT, B.M Oxfd M CH ORTH Lpool, F.R.C.S
of clinical studies and research and part-time o
surgeon, Robert Jones and Agnes Hunt Orthopædic
Oswestry

**Appointed Factory Doctors:**

BEETLES B N A, M B Madras Dagenham North, I
HENRY JOSEPH M.B Lond. Bradford West, York.
WARD, J A, M.R.C.S Syston, Leicester